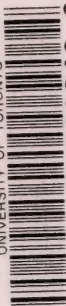



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# ANIMAL CHEMISTRY

WITH REFERENCE TO THE

## PHYSIOLOGY AND PATHOLOGY OF MAN

BY

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## EDITOR'S PREFACE.

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I HAVE much pleasure in presenting to the members of the Sydenham Society a translation of SIMON'S 'Chemistry of Man,'<sup>1</sup> a work that obtained for its author a European reputation, and is universally regarded as by far the most complete treatise that has yet appeared on Physiological Chemistry. Until I became acquainted with this work in 1843, I entertained the idea of publishing a text-book of medical chemistry with the view of attempting to supply a deficiency in the medical literature of this country, which, I doubt not, has been felt by many of my brethren as much as by myself. But a careful perusal of the 'Chemistry of Man' convinced me that I should be doing better service to the profession by undertaking a translation of that work than by the publication of a separate treatise. Impressed with this feeling I wrote to the author, who immediately offered me all the assistance in his power, and promised me a considerable amount of original matter. I regret to say that his early and unexpected death in the autumn of the same year rendered this promise of comparatively little value. I have, however, freely availed myself of the permission granted me by the Council of the Sydenham Society to insert such additions as the progress of chemistry, since the original

<sup>1</sup> Physiologische und pathologische Anthrochemie mit Berücksichtigung der eigentlichen Zoochemie. Berlin, 1842.

publication of the work, has rendered necessary. These interpolations, with the exception of one class, are distinguished by being included in brackets. I refer to the chemical essays of Simon, written with the view of filling up occasional deficiencies in his 'Chemistry of Man,' and published in his 'Beiträge zur physiologischen und pathologischen Chemie und Mikroskopie.' This exception was made at the request of Dr. Simon, and its expediency and fairness is unquestionable. The 'Chemistry of Man' was preceded by a volume entitled 'Chemistry of the Proximate Constituents of the Animal Body,' which, being in fact a distinct work, (containing upwards of 500 closely printed pages,) it has been deemed unadvisable to translate in its original form. A brief Introduction,<sup>1</sup> in a great measure based upon it, has been drawn up by myself, with the view of facilitating the perusal of the work to those who have not paid much attention to the recent progress of organic chemistry; and having written it with this object, I have intentionally excluded many topics which some of my readers may consider should have found a place there.

The following sketch of the life and writings of the Author, brief though it be, cannot be read without interest. It affords a striking illustration of the results that combined energy and talent are capable of evolving.

Franz Simon was the son of a surgeon residing at Frankfort on the Oder, and was born on the 25th of August, 1807. He distinguished himself at a very early age as a skilful apothecary; and, in volume 32 of 'Brandes's Archiv,' we find his essay on the preparation and properties of tinctures, to which one of the Hagen-Buchholz prizes was awarded in 1829. Even in this essay we can trace the germs of some of his future speculations in physiological chemistry. The following year he

<sup>1</sup> In the compilation of the Introduction I am likewise much indebted to Lehmann's 'Manual of Physiological Chemistry;' and to Mulder's 'Chemistry of Vegetable and Animal Physiology.'

obtained the first prize (the gold medal) for his essay on the best method of preparing infusions and decoctions (Brande's Archiv, vol. 35), a treatise equally remarkable for the extreme accuracy and care with which his experiments were conducted, and for the judgment displayed in his conclusions. In the year 1832 Simon came from the Rhine, where he had been practising as apothecary in different towns (Cleve, Düsseldorf, Cöln, and Deutz,) to Berlin, where he passed his examination as apothecary with the highest credit, and where, in addition to the practical department of his profession, he attended lectures on chemistry and pharmacy. He now published a small pamphlet entitled 'A brief Examination of Professor Kranichfeld's Treatise on the necessity of a Fundamental Knowledge of Pharmacy in relation to sound Medical Practice,' one of the most argumentative and powerful replies that Kranichfeld's absurd and unfounded accusation against the German apothecary system elicited. From this period till the year 1838 he devoted himself to study, having, with this view, given up his public pharmaceutical avocations in the year 1835. He attended, for six terms, lectures at the High School of Berlin, on natural history, physics, mathematics, history, and philosophy; he likewise published, conjointly with Dr. Meklenburg, a tabular view of chemistry (Berlin, Hirschwald.) Most of his leisure time at this period was devoted to toxicology, a subject on which he and his friend Dr. Sobernheim published a treatise which is regarded throughout Germany as the standard work on everything connected with poisons and poisoning. Some of the most important original investigations on which this work was based were originally published in Poggendorff's Annalen, vol. 40.

On the 3d of October, 1838, Simon received the degree of Doctor of Philosophy for his celebrated thesis '*De Lactis Muliebris ratione chemica et physiologica*,' which, in the course of the same year, was published, with considerable additions, in



the German language (*Die Frauenmilch*, u. s. w. Berlin, Förstner, 1838), and fully established his reputation as one of the most successful investigators of the age in the departments of organic chemistry and microscopy. It was regarded by Berzelius and others of our first chemists as the most perfect work on the subject of which it treats.

In 1839 his tabular 'View of the Mineral Springs of Europe, arranged with especial regard to their chemical composition and their physical and chemical characters' (*Die Heilquellen Europas*, u. s. w., Berlin, Förstner,) made its appearance, a work of very considerable labour, in which he collected and systematically arranged no less than 1045 analyses of European mineral waters; and in 1841 we find him an extensive contributor to Dr. Nicolai's 'Manual of Medical Jurisprudence,' having, in fact, executed the whole of the chemical and toxicological portion of the work. About this time the first part of the 'Chemistry of Man' appeared; it was not, however, completed till the summer of 1842, in consequence of Simon's determination to render the work as rich as possible in original analytical observations. With this view he was a constant attendant at Schönlein's clinical class, where his chemical services were highly valued, as manifested by the frequent reference made to them by that distinguished physician in his published Clinical Lectures. Scarcely had Simon concluded the 'Chemistry of Man' before he entertained the idea of editing a quarterly periodical devoted to his favorite pursuits, physiological and pathological chemistry. It appeared under the title of '*Beiträge zur physiologischen und pathologischen Chemie und Mikroskopie, in ihrer Anwendung auf die praktische Medizin.*' He lived to edit only three numbers. The fourth (edited by his friend Dr. Minding) contained the melancholy tidings of his death, which took place at Vienna on the 23d of October 1843, after an illness of only four weeks. Though no longer amongst us, the good that he did died not with him; his works, no



less than his example, have stimulated others to follow in his track, and to build upon the solid basis that he has left them. Even the very periodical that he commenced so shortly before his death is still conducted (under a different title) by an able chemist, and is producing results worthy of its original founder.

I gladly avail myself of this opportunity of expressing my obligations to the Council of the Sydenham Society for the promptitude with which they accepted my suggestion respecting the expediency of publishing an English edition of this work, and for intrusting me with the editorship of it; to one of that body, Mr. Ancell, I am very deeply indebted for the kind and valuable assistance that he has afforded me in the preparation of this volume for the press. Amongst the many other friends to whom my acknowledgments are due, I must especially mention Dr. Allen Thomson, Dr. Percy, Dr. Wright, and Dr. Golding Bird.

G. E. D.

*Southwick street, Hyde Park.*

## AUTHOR'S PREFACE.

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THE completion of the 'Chemistry of Man' has been unavoidably delayed beyond the time at which it was advertised to appear, in consequence of the large number of original analyses that I found it requisite to institute. As, however, these analyses materially increase the value of the work, I trust that my apparent procrastination will be readily forgiven. The present volumes comprise physiological and pathological chemistry. They treat of the physical and chemical relations of the fluid and solid portions of the human body in a state of health, and of the modifications they experience in different diseases. Moreover, in every instance, the chemical examination of the fluids and solids of the lower animals is appended to each chapter. The order in which the various matters treated in these volumes are discussed must be regarded rather as natural than physiological. After the circulating fluids, viz., the blood, lymph, and chyle, with which I commence,—I treat of the secreted and excreted fluids, as, for instance, those of the chylipoietic system, of the female breast, of the mucous membranes and skin, of the kidneys, &c.: next in order, I take the feces and vomited matters. I then consider the various tissues that enter into the composition of the animal body, as, for instance, the bones, muscles, skin, and glands; and I conclude with a description of various solid and fluid morbid products, such

as calculi, tubercular and carcinomatous matter, dropsical effusions, &c.

I have made myself practically conversant with the most approved methods of analysing the different fluids and solids described in this work; and, as far as my resources permitted, I have endeavoured to determine the various physical and chemical modifications they undergo in the course of different diseases. My attention has been especially directed to the study of those fluids that are of the greatest importance to the practical physician. Within the space of a few years I have made about 170 quantitative analyses of various animal matters, of which the very large majority refer to human blood, milk, and urine, and on which I lay the foundation for the pathological chemistry of those fluids. In fact, without these analyses it would have been impossible to publish a work worthy of the name of 'The Chemistry of Man;' for the essays of Andral and Gavarret on the Blood, and of Becquerel on the Urine, did not appear until I had made considerable progress in my work. I have deemed it, in every case, my duty to incorporate the results of other chemists with my own, and if, in any instance, I have failed in acknowledging the sources from which my statements have been drawn, the fault is one of inadvertence, not of design. All purely physiological matter, not bearing directly on chemistry, has been omitted; but microscopic investigation, especially in those instances in which it strengthens the evidence of experimental chemistry, has been deemed legitimately deserving of a place in this treatise.

My views regarding the metamorphosis of the blood, and its relation to nutrition and animal heat, were first communicated, at Erlangen in the autumn of 1840, to the medical and chemical section of Associated Naturalists; and my subsequent researches into the chemical constitution of the blood and urine confirm my belief in their general accuracy. These views may be summed up in the following terms: The blood is subjected

to a continuous metamorphosis, which may be regarded as the expression of its vitality. The nutrition of the peripheral system is effected by the liquor sanguinis, not by the blood-corpuscles. The liquor sanguinis affords nutriment to the cells and organs, which possess an inherent power of selecting proper material, or of forming it from non-homologous matter, at the same time secreting the products of decomposition. The principal nutritive matters in the liquor sanguinis are albumen, fibrin, and fat. The chief products of this metamorphosis are the extractive matters and lactic acid, which occur in the excretions, especially in the urine. Urea, bilin, and carbonic acid are either not products of the metamorphosis of the blood during the act of nutrition in the peripheral system, or at most they are only in part formed by it. They must be regarded as products of the vital energy of the blood-corpuscles, which, doubtless, possess the same power of attracting nutriment, and of throwing off decomposed products, as other living cells. The proper nutriment of these corpuscles is oxygen, albumen, and probably also fat, which are furnished them by the liquor sanguinis. The most important products of their metamorphosis are carbonic acid, urea, fibrin, extractive matters, and very probably some of the constituents of the bile. The leading and most important object of this vital energy of the blood-corpuscles is the production of animal heat, without which every function of the organism, nay even life itself, would be instantaneously annihilated. The production of animal heat is due to the combination of oxygen with the carbon of the globulin;<sup>1</sup> the principal products of this reaction are carbonic acid and urea, or uric acid, (which is excreted as a substitute for urea in most of those classes of animals in which elliptic blood-corpus-

<sup>1</sup> [Simon's views respecting the production of animal heat approximate closely to those expressed by our countryman, Mr. Ancell, in his 11th lecture on the blood. See *Lancet*, 1840, vol. i. p. 829, or Dr. Posner's German edition of the collected lectures, p. 200.]



cles occur.) The urea excreted may thus be regarded as a measure or equivalent of the animal heat developed.

The production of blood-corpuscles and the formation of blood are intimately connected with nutrition : when the food is too scanty and insufficient, the amount of blood, and especially of blood-corpuscles, is diminished ; when the nutriment is proper and abundant, the reverse takes place. In the former case, therefore, the vital energy is depressed, the secretions and excretions are diminished, and the animal heat sinks ; while in the latter case exactly the reverse is observed. In the normal state there is an equilibrium preserved between the production and consumption of blood-corpuscles. The food is prepared, and to a certain extent assimilated, before it enters the blood. The vital energy of the blood-corpuscles continues even during a perfect abstinence from food, and carbonic acid and urea continue to be formed, although their amount gradually diminishes in a direct ratio with the diminution of the blood-corpuscles.

Moreover, the amount of carbonic acid and the formation of urea are lessened by a torpid, and increased by an excited circulation ; and in proportion to the amount of corpuscles and to the rapidity of the circulation, so much the higher is the animal temperature. Thus in birds we observe a high temperature, and the reverse in the amphibia. In chlorotic, and also in very aged persons we find a low temperature, and a diminished excretion of urea, while in inflammatory diseases, and after prolonged corporeal exertion the temperature rises, and there is either a relative or an absolute increase of urea ; in the former case, even in the absence of all nitrogenous food. The capillary and cutaneous systems tend to regulate an excessive rapidity of the circulation, and to prevent the animal heat from exceeding a certain limit.

If we only knew whether, and in what manner, the pulmonary exhalation is changed in various diseases, (especially in relation to the amount of carbonic acid contained in it,) whether

the carbonic acid always increases relatively with the urea, or in certain cases with the uric acid, and if further, we possessed experiments illustrative of the effects of diseases, and of varied diet on the bile, we should then have a more solid basis than we now occupy, on which to found our chemical inquiries, while the acquisition to the science of medicine would be positive and incalculable. The questions here involved must, however, unfortunately, at the present time, be regarded as unanswerable. We cannot doubt that the pulmonary exhalation does vary, under different circumstances, in the amount of carbonic acid; for instance, more carbonic acid is exhaled during prolonged corporeal exertion than when the body is in a state of repose; although, as far as I am aware, no experiments on this subject have yet been instituted.<sup>1</sup> We have, however, conclusive evidence that the amount of urea is increased under these circumstances.

On the other hand, in the researches of Trommer regarding the passage of sugar into the portal blood of horses, this substance could not be detected in the chyle nor in the arterial or venous blood, which renders it more than probable that the liver not only serves the purpose of modifying the composition of the blood, but likewise effects the object of altering or removing abnormal substances from it that have been absorbed by the mesenteric veins. Hence this organ appears, in a certain degree, to take a share in the process of digestion, an opinion supported by Berzelius. Future investigations respecting the functions of the liver may lead to very important results, and throw much light on many of the most obscure departments of physiology.

Although very little has yet been done in physiological and pathological chemistry, the rational physician, who ventures to cast aside the trammels of dogmatism and empiricism, cannot,

<sup>1</sup> [The experiments of Scharling on this subject were made after the publication of the 'Chemistry of Man.' A brief notice of them is given in p. 129 of this volume.]

for an instant, doubt that pathology, therapeutics, and diagnosis, are only safely based on chemistry, physiology, and morbid anatomy: he cannot entertain a doubt that the same chemistry with which he scans the changes in crude inorganic matter, will likewise enable him, if not at present, yet surely at some future period, to detect the variations in the composition of the animal fluids and solids, some of which are dependent on physiological, others on pathological causes, and will throw a new light on the normal functions of the organism, as well as on the various processes of disease.

After contemplating the dependence of vital manifestations on the unceasing metamorphosis of the animal body, and the secretions and excretions as its products; after glancing at the physical and chemical modifications that these secretions and excretions undergo in numerous pathological conditions, and observing how these changes affect the structure and chemical conditions of the different organs, we can no longer entertain a doubt that all morbid phenomena are accompanied by metamorphoses in the organism, different from those that occur in the normal condition. But it will require an immense number of analyses in order to ascertain and determine these modifications, to express them in definite terms, to connect them duly with functional disturbances in the organism, or with other symptomatic phenomena; and, finally, as far as possible, to endeavour to discover their origin. In such researches the mere chemist can do little: in order to produce results really serviceable to science, physiology and pathology are as essential as chemistry itself, and no one can hope to advance this department of scientific inquiry who does not include, in his own person, the chemist, the physiologist, and the pathologist.

Every science is slowly and gradually developed. Physiological and pathological chemistry forms no exception to this rule: it is still a mere infant science, that has scarcely attained a self-dependent existence. The reader must therefore not

require of this work more than the present state of the science will enable me to present him with. He will find in it chemical facts which the physiologist and pathologist may render of further service: the few scattered ideas concerning the metamorphosis of the blood, and the probable connexion between various diseases and certain modifications in the composition of the different animal fluids, may serve as connecting links for further investigations.

The materials for my analyses have been chiefly derived from the Charité (hospital) of this city, from some of the public cliniques, from private practice, and from the royal veterinary school. I gladly avail myself of this opportunity of publicly expressing my thanks to Drs. Schönlein, Wolff, and Romberg, as well to Professors Gurlt and Hertwig, and the other professional friends who have favoured me with their advice and assistance. I must likewise express my obligation to Dr. v. Behr, who assisted me for a considerable time in my researches on the urine.

That this work may succeed in encouraging a taste for a department of science, whose cultivation and further development is, at the present time, imperatively demanded by the medical public, is the most sincere wish of

THE AUTHOR.

BERLIN, *April* 1842.



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# CHEMISTRY OF MAN.

## INTRODUCTION.

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THE proximate constituents of the animal body may be divided into two great classes, the *mineral* and the *organic*; each of which admits of several sub-divisions.

### I. MINERAL CONSTITUENTS.

The *Mineral Constituents* may be advantageously classed in three groups, comprising, I, Those which are of service in the animal body, in consequence of their physical properties; II, Those which effect important objects in the system by their chemical actions; and III, Those which, being only incidentally present, may be eliminated without exerting any unfavorable effect on the economy.

#### CLASS I. CONSTITUENTS USEFUL BY THEIR PHYSICAL PROPERTIES.

1. *Water*. This substance is so universally diffused, and its uses are so obvious as to render any observations unnecessary.

2. *Phosphate of lime*, in the importance of its physical properties to the animal organism, undoubtedly ranks next to water. Phosphate of lime or, as it is often termed, bone-earth, consists of 8 eq. of lime and 3 eq. of phosphoric acid; its empirical formula therefore is  $8 \text{ Ca O} + 3 \text{ PO}_3$ ; but there can be no doubt that

it is a compound of two tribasic phosphates of lime, namely  $2 \text{ Ca O, HO, PO}_5 + 2 (3 \text{ Ca O, PO}_5)$ . It consists of 51.55 parts of lime, and 48.45 of phosphoric acid. It occurs in bone, blood, milk, urine, fæces, &c.

3. *Carbonate of lime* forms the principal part of the skeleton in the invertebrata; it also occurs in greater or less proportion in the bones of the higher animals and man, in the urine of the gramminivora, and in certain morbid concretions. It contains 56.29 parts of lime and 43.71 of carbonic acid.

4. *Phosphate of magnesia* is very frequently associated with phosphate of lime. In a crystalline state its formula is  $\text{H O, } 2 \text{ Mg O, PO}_5 + 2 \text{ H O} + 12 \text{ H O}$ . (Graham in Phil. Trans. 1837.) It occurs in bone, blood, milk, shell of eggs, urine of man and carnivora, intestinal concretions, fæces, &c. After the removal of the water of crystallization it consists of 36.67 parts of magnesia, and 63.33 of phosphoric acid.

*Phosphate of magnesia and ammonia*, or, as it is frequently termed, *ammoniaco-magnesian phosphate*, is a perfectly distinct salt. Like the former, it is a tribasic salt, of which the 3 atoms of base are, 1 atom of oxide of ammonium, and 2 atoms of magnesia, with 12 atoms of water of crystallization, 10 of which may be expelled without any loss of ammonia. Its formula therefore is  $\text{NH}_4 \text{ O, } 2 \text{ Mg O, PO}_5 + 2 \text{ HO} + 10 \text{ HO}$ . Crystals of this salt have been observed in the excrements in typhus and other diseases; it is also present in certain states of the urine, and is a frequent constituent of urinary calculi.

5. *Fluoride of calcium* occurs in the animal organism in very minute quantity. It is much more abundant in fossil than in recent bones.

#### CLASS II. CONSTITUENTS USEFUL BY THEIR CHEMICAL PROPERTIES.

1. *Hydrochloric acid* exists in the digestive fluid of man, of the mammalia generally, and of birds. It has been detected by Lehmann in morbid saliva.

2. *Hydrofluoric acid* has only been detected in the gastric secretion of birds.

3. *Chloride of sodium* exists in the blood, gastric juice, urine, bone, cartilage, &c.

4. *Carbonate of soda* is a very common ingredient in the ash of animal substances; in most cases it is derived from compounds of soda with organic acids, especially lactic acid. It is also found in the urine of the graminivora.

5. *Phosphate of soda* occurs in the blood, lymph, chyle, bile, milk, and urine. Its formula is  $\text{HIO}, 2 \text{NaO}, \text{PO}_5 + 24 \text{HIO}$ . On the addition of muriate of ammonia to a solution of this salt, we obtain the "sal microcosmicus" of the older chemists, which is found in considerable quantity in decomposed animal fluids; its formula is  $\text{HIO}, \text{NH}_4 \text{O}, \text{NaO}, \text{PO}_5 + 8 \text{HIO}$ . The recent investigations of Enderlin tend to prove that the phosphate of soda that most commonly occurs in the animal fluids and tissues, contains 3 atoms of soda, and may be represented by the formula  $3 \text{NaO}, \text{PO}_5$ .

6. *Chloride of calcium* is found in the gastric juice and saliva.

7. *Chloride of iron* (apparently the proto-salt) occurs in the gastric juice.

8. *Iron* is found in considerable quantity in *hematin*, the principal colouring matter of the blood; also in lymph, chyle, black pigment of the eye, hair, &c. In what state it exists, whether as a peroxide or protoxide, or either, is not known. It is also found in lesser proportion in bile, urine, sweat, milk, &c. In some of these fluids it is stated to exist as a phosphate.

#### CLASS III. INCIDENTAL CONSTITUENTS.

1. *Chloride of potassium* is found in almost all the animal fluids.

2. *Alkaline sulphates* occur in small quantity in most of the animal fluids, in the blood, milk, urine, and sweat. Mitscherlich could not detect any alkaline sulphates in the saliva, and Lehmann has recently shown that they do not *exist* in the bile, although they may be *produced* in the ash.

3. *Carbonate of magnesia* has been found in alvine concretions, urinary calculi, &c., in man and the mammalia. It occurs in considerable quantity in the urine of the graminivora, and is a constituent of the shell of the egg. Berzelius suggests the probability of magnesia being contained in bone, not as a phosphate but as a carbonate, and that the phosphate of magnesia is produced during analysis.

4. *Manganese* has been found in the hair; it has also been

detected in human gall-stones, (in one instance there was found as much as  $0.3\frac{0}{10}$  of the protoxide of manganese,) and traces of it have been observed in the urinary calculi of the graminivora.

5. *Silica* has been found in small quantity in the enamel of the teeth, in bone, urine, urinary, intestinal, and biliary calculi, hair, and saliva. It is found in considerable quantity in the excrements, the amount varying with the nature of the food. In the sheep the excrements have been observed to contain as much as  $6.0\frac{0}{10}$  of silica.

6. *Alumina*. Traces of this substance were detected by Vauquelin, in human bones; it has been found in considerable quantity in fossil teeth and horns. The circumstance of its being an occasional constituent of intestinal concretions coincides with Lehmann's experiments, in which he found that when alumina was introduced into the system, it was carried off by the feces.

7. *Arsenic* was recently stated by Orfila to be a normal constituent of human bone. This opinion has, however, since been withdrawn, and there is little doubt that there was some fallacy in his experiments.

8. *Copper* is considered by Devergie, Lefortier, and Orfila, to be a normal constituent of all the soft parts, as well as of the blood of healthy persons. Devergie<sup>2</sup> analysed the viscera of five persons and found it in every instance. It has also been found in the sweat.

9. *Lead* has been found by these chemists in the same cases as copper.

10. *Ammoniacal salts*. In the blood, lymph, chyle, and milk, there are no appreciable ammoniacal salts. They have been observed in some cases in the sweat, and they occur in a small proportion in the urine.

<sup>1</sup> The notation  $\frac{0}{10}$  represents per centage.

<sup>2</sup> These observations have recently been confirmed by M. Barse, who succeeded in finding both copper and lead in the bodies of two persons to whom they could not have been given for poisons. It seems from the analyses of Signor Cattanei that neither of these metals exists in the bodies of new-born children or infants; and Rossignon has recently pointed out the sources from which the bodies of adults probably derive their copper. He has found this metal in gelatin, chocolate, bread, coffee, sugar, &c.



## II. ORGANIC CONSTITUENTS.

The *Organic Constituents* may be arranged in two principal groups, the former embracing the nitrogenous, the latter the non-nitrogenous matters. In the nitrogenous group we have protein, and its various modifications—gelatin, bilin, and the products of its metamorphosis—hematin, urea, uric acid, &c.: in the non-nitrogenous we place the animal sugars, fats, lactic and acetic acids, &c. &c.

## CLASS I. NITROGENOUS CONSTITUENTS.

1. *Protein*.

Under this head we shall consider three very important compounds which are formed in the vegetable kingdom, and which are also found to constitute the greater part of the animal body. These are Albumen, Fibrin, and Casein. Two most important discoveries have recently been made regarding these substances. The first is the discovery made by Mulder that albumen, fibrin, and casein are nothing more than modifications of one compound to which he has given the name of *Protein*, (from  $\pi\rho\omega\tau\epsilon\upsilon\omega$ , I am first,) which may be regarded as the commencement and starting-point of all the tissues: the second is, that protein, in every respect identical with that which forms the basis of the three aforesaid animal principles, may be obtained from similar elements in the vegetable kingdom. When the newly-expressed juices of vegetables are allowed to stand, a separation takes place in a few minutes. A gelatinous precipitate commonly of a green tinge is deposited, and this, when acted on by liquids which remove the colouring matter, leaves a grayish white substance, which has been named *vegetable fibrin*. It separates from the vegetable juice in which it was originally dissolved exactly as fibrin does from blood.

When the clarified juice of nutritious vegetables, such as cauliflower, asparagus, mangel-wurzel, or turnips, is made to boil, a coagulum is formed which it is absolutely impossible to distinguish from the substance which separates as a coagulum, when the serum of blood, or the white of an egg, diluted with water, is heated to the boiling point. This is *vegetable albumen*.

*Vegetable casein* is chiefly found in the seeds of peas, beans, lentils, and similar leguminous seeds. Like vegetable albumen, it is soluble in water, but differs from it in this, that its solution is not coagulated by heat. When the solution is heated or evaporated, a skin forms on its surface, and the addition of an acid causes a coagulum just as in animal milk.

“The chemical analysis of these three substances has led to the very interesting result that they contain the same organic elements united in the same proportion by weight; and what is still more remarkable that they are identical in composition with the chief constituents of blood, animal fibrin and albumen.

They all three dissolve in concentrated muriatic acid, with the same deep purple colour, and even in their physical characters animal fibrin and albumen are in no respect different from vegetable fibrin and albumen. It is especially to be noticed, that by the phrase identity of composition we do not here imply mere similarity, but that, even in regard to the presence and relative amount of sulphur, phosphorus, and phosphate of lime, no difference can be observed.”<sup>1</sup>

When animal or vegetable albumen, fibrin, or casein is to be used for the extraction of protein in a state of purity, the following steps are to be taken. The selected substance is successively washed with water, alcohol, and ether, for the purpose of removing extractive matter, fat, and soluble salts. It is then treated with dilute hydrochloric acid, which extracts the phosphate of lime and any other insoluble salts that may happen to be present. We now dissolve it in a moderately strong solution of caustic potash, and keep the solution for some time at a temperature of 120°, whereby the sulphur and phosphorus that are present form phosphate of potash and sulphuret of potassium.

The protein is then to be thrown down from the solution, after filtration, by acetic acid, which must be added only in very slight excess, as otherwise the precipitate would be redissolved. It must then be collected on a filter and carefully washed till every trace of acetate of potash is removed.

In this state it occurs in the form of grayish white gelatinous flocks, which, when dried, become hard and yellow, and give an amber-coloured powder. It is insoluble in water, alcohol, and

<sup>1</sup> Liebig's Animal Chemistry, translated by Gregory; p. 47.

ether, and is devoid of odour and taste. It readily absorbs moisture, and swells up, but regains its original form upon being heated to  $212^{\circ}$ .

Mulder has analysed protein from animal and vegetable albumen, from fibrin, and from cheese or casein; Scherer has analysed it from animal albumen and fibrin, from the crystalline lens, from hair, and from horn; and Dumas from animal albumen and casein.

The formulæ which these chemists have assigned to it approximate closely to each other, although they are not absolutely identical. As Mulder's original formula has been confirmed by the recent investigations of Schröder and Von Laer, we shall adopt it as the correct symbol of the composition of this substance. According to this view the composition<sup>1</sup> of an atom of protein is represented by the formula  $C_{40} H_{31} N_5 O_{12}$ . Its atomic weight is 5529.5, oxygen being 100, and its symbol is  $\overline{Pr}$ . It burns when exposed to the air, without leaving any ash. When boiled for a considerable time in water, with free exposure to the air, protein becomes slowly oxydised. We shall revert to this subject presently.

Protein combines both with acids and bases. It dissolves in all very dilute acids, and forms with them a kind of neutral compound, which is insoluble or nearly so when there is an excess of the acid present. Hence if sulphuric, hydrochloric, or nitric acid be added to a solution of protein in a dilute acid, the protein is precipitated in an insoluble state; if however the excess of acid is removed by careful washing, the precipitate becomes again dissolved. Acetic acid and the ordinary (tribasic) phosphoric acid constitute an exception to this rule as they dissolve protein in all proportions. Protein may be precipitated from any of its acid solutions by ferrocyanide and ferridecyanide of potassium, by tannin, by anhydrous alcohol, by various metallic salts, and by the alkalies.

*The Metamorphoses of Protein.* a. *Sulphuric acid and protein.* On the addition of concentrated sulphuric acid to protein or to any of its modifications (albumen, fibrin, or

<sup>1</sup> Liebig's formula for protein is  $C_{48} H_{36} N_6 O_{14}$ . The numerical results afforded by these formulæ approximate very closely. See Appendix I, Note 1.

casein) a gradual swelling ensues, and the substance assumes a gelatinous appearance. On the addition of water it contracts, and it is found to be perfectly insoluble in that fluid. It must be collected on a filter and boiled in water as long as a solution of baryta indicates that any sulphuric acid is being given off: it must then be heated with alcohol, and dried at a temperature not exceeding  $260^{\circ}$ . This is *sulpho-proteic acid*. It appears as a yellow mass, is not easily pulverized, and is insoluble in water, alcohol, and ether, but dissolves in potash and ammonia. The salts of silver, copper, lead, and iron yield precipitates with the alkaline solutions of this acid. Its formula is  $C_{24} H_{31} N_5 O_{12}, SO_3$ .

On the cautious addition of dilute sulphuric acid to an acetic acid solution of protein, we obtain Mulder's *sulpho-bi-proteic acid*, which is then thrown down as a flocculent precipitate. After washing it, and drying it at a temperature not exceeding  $260^{\circ}$ , it assumes a white appearance, and may be easily pulverized. With the alkalies it forms solutions from which many of the metallic salts throw down insoluble compounds. Mulder considers that it is composed of two atoms of protein, two of water, and one of sulphuric acid; hence it may be expressed by the formula  $C_{80} H_{62} N_{10} O_{24} + H_2 O_2 + SO_3$ .

If protein (or any of its modifications) be boiled in dilute sulphuric acid, a beautiful purple tint is evolved.

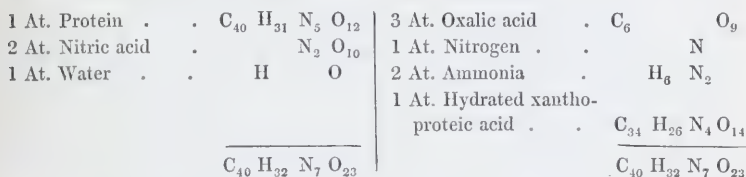
*β. Hydrochloric acid and protein.* Mulder has formed a *hydrochloro-proteic acid* in the same manner as the sulpho-proteic acid. Its formula is  $C_{80} H_{62} N_{10} O_{24} + H_2 O_2 + H Cl$ . When protein is boiled in strong hydrochloric acid the solution is at first yellow, but it gradually merges into a blue tint. This change of colour does not occur if the atmospheric air is excluded.

*γ. Nitric acid and protein.* On the addition of nitric acid to protein or to any of its modifications, nitrogen and a little nitric oxide are evolved, oxalic acid and nitrate of ammonia are formed, and there remains undissolved a bright yellow matter, which on being dried assumes an orange tint, and which is known as *Xantho-proteic acid*. It is devoid of smell and taste, although it slightly reddens moistened litmus paper. It is insoluble in water, alcohol, and ether. It dissolves in strong mineral acids, but is precipitated on the addition of water; with the



alkalies it forms dark red soluble salts, and metallic salts throw down yellow precipitates. In a state of combination, the formula for this acid is  $C_{34} H_{24} N_4 O_{12}$ ; when free it contains two atoms of water.

The changes which occur in the production of this acid may be illustrated by the equation—



δ. *Chlorine and protein.* On passing a current of chlorine gas through a solution of any of the protein-compounds, (albumen, fibrin, or casein,) a white flocculent precipitate is thrown down. After washing it, and carefully drying it at a temperature of 212°, Mulder deduced from it the formula  $C_{40} H_{31} N_5 O_{12} + Cl O_3$ . He termed it *chloro-proteic acid*. It appears from his investigations that the protein remains unchanged, but that a portion of the water is decomposed, and that its oxygen combines with chlorine to form chlorous acid ( $Cl O_3$ ) while its hydrogen combines with another portion of chlorine to form hydrochloric acid ( $H Cl$ ) which remains in solution in the water.<sup>1</sup>

When ammonia is added to the chlorod-proteic acid, the latter substance dissolves, and gives off a large amount of nitrogen. The solution must be evaporated to dryness, and then treated with warm water, which takes up a portion of the residue. On the addition of alcohol to this aqueous solution, a precipitate is thrown down, while muriate of ammonia remains in solution. This precipitate is composed of a substance of great physiological interest. Its formula<sup>2</sup> is  $C_{40} H_{31} N_5 O_{15} + HO$ . Mulder originally termed it *oxyprotein*, but he has recently given it the more descriptive name of *tritoxide of protein*, without however intending to imply anything more than that it contains three atoms more oxygen than protein. There is another and, in

<sup>1</sup> That this compound is a chlorite of protein and not a chloride of tritoxide of protein seems certain from its analogy with a corresponding compound of gelatin.

<sup>2</sup> See Appendix I, Note 2.

theory, a simpler method of obtaining this compound. When fibrin or albumen of inflamed or healthy blood, of serum of the blood, or of hen's eggs, is boiled with water, after four hours' boiling, principles are always obtained which are soluble in water, whilst the greater part remains undissolved. On repeating the ebullition every four hours with fresh water, fresh quantities of soluble matter are extracted, the insoluble portion becoming poorer in carbon, hydrogen, and nitrogen, but richer in oxygen, until the composition is finally constant. Moreover, the portion of albumen or fibrin soluble in water when evaporated, extracted with alcohol, and treated with cold water, is almost entirely soluble in it, and likewise contains less carbon, hydrogen, and nitrogen, but more oxygen than protein. The substances taken up by the alcohol are merely products of decomposition of the soluble portion of the fibrin or albumen. It is, moreover, the decomposition of this portion that gives rise to the ammonia that is produced on distilling albumen or fibrin with water.

The soluble matter taken up from the fibrin or albumen by prolonged ebullition is in every respect identical with the tritoxide of protein which we have already described; it exists moreover ready-formed in the buffy coat of the blood. From whichever of these sources we procure it, whether from chloroproteic acid, from albumen or fibrin, by prolonged ebullition, or from the buffy coat of the blood after a comparatively short ebullition, it possesses the same properties. It is soluble in cold water, but not in ether, alcohol, essential or fat oils; it has neither an acid nor alkaline reaction. It is always precipitated in the same manner from its aqueous solution by diluted nitric, sulphuric, hydrochloric, neutral and basic phosphoric, and tannic acids; by solutions of chlorine, bichloride of mercury, neutral and basic acetate of lead, nitrate of silver, sulphate of zinc, and peroxide of iron. It forms with metallic oxides a class of double salts, which are composed according to the formula  $(C_{40}H_{31}N_5O_{15} + MO) + (C_{40}H_{31}N_5O_{15} + HO)$ .

Tritoxide of protein is not precipitated by dilute acetic acid, neutral salts of potash and soda, chloride of barium, hydrochlorate of ammonia, nor by that very delicate test for protein, ferrocyanide of potassium. It dissolves gradually in solutions of potash, soda, and ammonia. When thoroughly dried, it occurs as an amber-coloured powder. Nitric acid converts it into

xantho-proteic acid, a change which is not produced by the action of that reagent upon chlorod-proteic acid.

Let us now revert to the undissolved residue, which ultimately assumes a uniform composition expressed by the formula<sup>1</sup>  $C_{40} H_{31} N_5 O_{14}$ . It is this which is first formed from protein by the influence of the oxygen of the atmosphere. The other substance (trioxide of protein) originates from it by the addition of another equivalent of oxygen. In this respect albumen and fibrin give different results. Albumen, without going through this preparatory change like fibrin, is at once converted into trioxide of protein by ebullition, the insoluble portion which remains being unaltered albumen.

From the composition of this insoluble portion it has received the name of binoxide of protein. It exists ready formed in the buffy coat of the blood. Von Laer has obtained it from hair in the following manner. The protein is first thrown down by the addition of a little acetic acid to a solution of hair in potash. On the addition of a larger proportion of free acid, after the removal of the protein, another substance, previously in a state of solution, is thrown down. This is the binoxide of protein. Von Laer describes it as a bright yellow precipitate. After being carefully washed and dried it forms a black, glossy resinous mass, which on being pulverized forms a dark amber-yellow powder.

It is insoluble in water and alcohol, but dissolves perfectly in dilute acetic, hydrochloric, nitric, and sulphuric acids. It does not assume so strong a yellow colour as protein, when treated with nitric acid.

Ferrocyanide and ferridcyanide of potassium, and acetate of lead precipitate it from its acid solutions. It is soluble in potash and ammonia.

If the binoxide of protein be treated with chlorine there is formed, at a loss of one atom of nitrogen, and a gain of three of oxygen, a new substance  $C_{40} H_{31} N_4 O_{17}$ , to which no name has yet been assigned.

In order to obtain these products of oxidation of protein by boiling fibrin in water, it is essentially necessary that there should be free access to the atmospheric air.

<sup>1</sup> See Appendix I, Note 3.

The products of the oxidation of protein occur constantly in the blood; they are formed in the lungs from fibrin, a substance which has been shown by Scherer to possess the property of absorbing oxygen when in a moist state. The fibrin, oxidised in the lungs is, according to Mulder, the principal, if not the only, carrier of the oxygen of the air; it is especially this substance from which the secretions are formed.

In inflammatory conditions, a considerably larger quantity of protein in an oxidised state, is contained in the body, than is found in a normal state.<sup>1</sup>

These compounds (or at least one of them) are also found in pus, the substance termed *pyin* being in reality tritoxide of protein; in false membranes, in cooked meat, and in vitelline substance; in the last-named substance we meet with a sulphuret of the binoxide of protein.

Mulder has recently obtained a third oxide of protein, represented by the formula  $C_{10}H_{31}N_5O_{20}$ , by boiling yeast in water. It occurs in a state of solution.

<sup>1</sup> The examination of the foregoing facts leads to some very important conclusions. We see, for instance, that, by the ebullition of meat, protein is converted into two oxides, and is thus no more presented to the organism as a means of nutrition in the form of protein, but one part is converted into binoxide, which is hard and sparingly soluble, while another portion is changed into the soluble tritoxide, and occurs in broth, extract of meat, &c. According to Mulder, the interior of roasted meat undergoes a change analogous to that which is produced by ebullition. As the effects of ebullition upon albumen differ from those on fibrin, in evolving only the tritoxide of protein, boiled albumen must be perfectly distinct from boiled or roast meat as a means of nourishment.

The process of inflammation also appears essentially as a higher grade of oxidation. The albumen of the blood, which furnishes only tritoxide by ebullition, probably takes no part in the change: we may conclude that it is effected by the fibrin alone, which, as we know, absorbs oxygen from the air, and is with so much comparative facility converted into binoxide and tritoxide of protein. During the height of inflammation, there is a great excess of the oxides of protein in the blood; in a state of health they are, doubtless, present, but in much smaller proportions. Between these extremes there may be many intermediate states induced by different disorders. Respiration may consequently be regarded as a true oxidation of the blood, or rather of the protein; and in inflammation, in which the blood contains a greater quantity of binoxide and tritoxide of protein than in the healthy state, this body becomes more thoroughly oxidised. Hence it occurs that, in the acceleration of the act of respiration, in fevers, for example, inflammation so easily supervenes after any violent or sustained efforts. Every paroxysm of fever must necessarily cause the formation of a greater quantity of oxidised protein in the system, and every augmen-



ε. *Potash and protein.* On the addition of protein to a concentrated solution of potash, and submitting the mixture to ebullition decomposition takes place, and a crystalline substance, two distinct extractive matters, and formate and carbonate of ammonia are produced. After the alkaline solution has been neutralized as completely as possible by sulphuric acid; the formic acid may be removed by gentle distillation.

On evaporating the mixture to about one third of its volume, the greater part of the sulphate of potash will separate in a crystalline state.

After its removal, the fluid which is of a reddish brown colour must be reduced to the consistence of an extract, and then treated with boiling alcohol, which will take up everything except any sulphate of potash that may have escaped previous removal. As the alcoholic solution cools, *erythroprotid* is deposited, in the form of a reddish brown extract. It is readily soluble in water, and in boiling, but not in cold, alcohol; and it is precipitable from its aqueous solution by the salts of lead, silver, and mercury, of a rose-red colour: it is also precipitable by tannic acid. From an analysis of the combination of erythroprotid with oxide of lead, Mulder has estimated its composition<sup>1</sup> at  $C_{13} H_8 N O_5$ .

Subsequently to the deposition of erythroprotid, *leucin* separates in a crystalline state. It occurs in brilliant plates or scales, somewhat resembling cholesterin. It cranches between the teeth, is inodorous and tasteless, and sublimes unchanged

tation in the amount of oxidised protein must produce inflammation, which may in its turn determine fever. Hence also it happens that stimulating foods and drinks, which quicken the respiration, or cold air, which introduces more oxygen into the lungs, often give the first impulse to the development of inflammation in the organism. The buffy coat is formed when the oxides of protein predominate in the blood; when they accumulate in any particular part of the system, local inflammation is the result. In the latter case, morbid products, *e.g.* false membranes, &c., are evolved, which are found on analysis to be in a great measure composed of oxidised protein. Now inflammation must be combated by endeavouring to diminish the quantity of the tritoxide of protein, and to hinder its formation in the lungs. Venesection proves antiphlogistic by directly diminishing the tritoxide of protein: increased secretion of the alimentary canal indirectly produces the same effect by accelerating the change of substance in the body, and consequently also the consumption of a greater quantity of protein and its oxides.

<sup>1</sup> See Appendix I, Note 4.

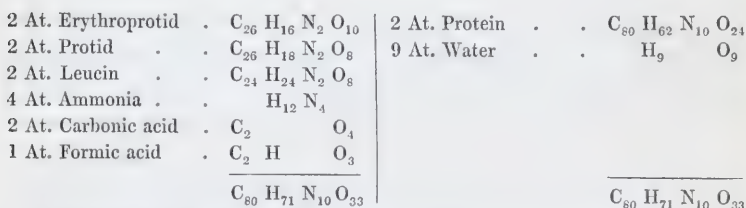
at about  $340^{\circ}$ . It contains no water of crystallization. It is soluble in water and in alcohol, but not in ether: its formula<sup>1</sup> is  $C_{12} H_{12} N O_4$ . According to Mulder it must be regarded as an integral constituent of protein. It combines with nitric acid and forms a crystalline acid to which the term nitro-leucic acid has been given.

We shall have occasion to revert to leucin in our observations on gelatin.

*Protid* is the term applied to the extractive matter that remains in solution after the removal of the *erythroprotid* and *leucin*. It is of a bright yellow colour, easily pulverizable, and soluble in water and alcohol without colouring them. It is precipitable by the basic acetate of lead, but not by any other metallic salts nor by tannin. The salts of lead serve to distinguish it from erythroprotid. If a mixture of these two substances be dissolved in water, the latter is precipitated by the neutral, the former by the basic acetate of lead.

Its formula<sup>2</sup> is  $C_{13} H_9 NO_4$ .

The action of caustic potash on protein is evidently very complicated. Mulder endeavours to show by the following formula how these metamorphoses *may* occur.



According to Liebig, protein is produced by vegetables alone, and cannot be formed by animals, although the animal system has the power of converting one modification of protein into another; it is never found *as protein*, in nature; but occurs in the shape of albumen, fibrin, or casein, both in vegetables and animals. These modifications of protein are employed in the formation of the different tissues, each of which bears a simple relation to that substance, as will be seen by the following table:—

<sup>1</sup> See Appendix I, Note 5.

<sup>2</sup> *Ib.* Note 6.

Albumen of the blood	.	.	.	$= 10 \overline{\text{Pr}} + \text{S}_2 \text{P}$
Albumen of the egg	.	.	.	$= 10 \overline{\text{Pr}} + \text{S P}$
Fibrin	.	.	.	$= 10 \overline{\text{Pr}} + \text{S P}$
Casein	.	.	.	$= 10 \overline{\text{Pr}} + \text{S}$
Globulin	.	.	.	$= 15 \overline{\text{Pr}} + \text{S}$
Muscular flesh	.	.	.	$= \overline{\text{Pr}} + \text{H O} + \text{H}$
Arterial membrane	.	.	.	$= \overline{\text{Pr}} + 2 \text{H O}$
Mucus	.	.	.	$= \overline{\text{Pr}} + 3 \text{H O}$
Chondrin	.	.	.	$= \overline{\text{Pr}} + 4 \text{H O} + 2 \text{O}$
Horny tissue	.	.	.	$= \overline{\text{Pr}} + \text{N H}_3 + 3 \text{O}$
Gelatinous tissue	.	.	.	$= 2 \overline{\text{Pr}} + 3 \text{N H}_3 + \text{H O} + 7 \text{O}$

We do not mean to assert that these formulæ represent the actual constitution of the respective tissues, but only that they give the proportion of elements actually present, and show how they might give rise to those tissues. Some of these tissues contain protein, or at least yield it by the action of potash, whilst others, as for instance the gelatinous tissues, although doubtless derived from protein compounds, do not contain it, and consequently cannot yield it.

*Diagnosis of protein.* Its insolubility in water, alcohol, and ether, and its precipitation from an acid solution by the ferrocyanide and ferrideyanide of potassium are sufficient.

## 2. Albumen.

This important modification of protein forms the white of eggs, and occurs in large quantity in all the animal fluids that contribute to the nutrition of the organism. It is also found in most of the animal solids, and in nearly all morbid products. We have already adverted to its existence in the vegetable kingdom.

Albumen is naturally soluble in water, and it is found dissolved in the serum of the blood, in vegetable juices, &c. But when it has once been submitted to a certain degree of temperature, or to the action of various chemical reagents, it assumes the coagulated state, and becomes insoluble in water.

*Soluble albumen.* Soluble albumen may be obtained in a solid form by evaporating to dryness, at a temperature not exceeding  $120^\circ$ , the serum of the blood, or white of egg. The dry mass is yellow, partially transparent, hard, and tough; it must

be reduced to a fine powder, and treated successively with ether and alcohol. By these means we succeed in removing nearly all foreign bodies from the albumen, which when dried exhibits a white or pale yellow colour, is devoid of taste and odour, and presents a neutral reaction. If perfectly dry, albumen in this state may be exposed to a temperature of  $212^{\circ}$  without passing into the coagulated condition. When digested in cold water, it gradually swells up, and finally dissolves, forming a mucilaginous, colourless, and insipid fluid, which on being heated to  $140^{\circ}$  begins to give indications of coagulating: if the solution is very dilute, the temperature may be raised to  $165^{\circ}$  with the occurrence of this change, and when present in very small quantity the albumen may not separate till the fluid boils, or even until the ebullition has been prolonged for a short time.

When albumen is analysed, it yields the same results as protein in regard to carbon, hydrogen, nitrogen, and oxygen, but it also contains a small quantity of phosphorus and sulphur, (less than 1% together,) which are absent in protein. According to Mulder's analyses,<sup>1</sup> the albumen of eggs may be represented by the formula  $C_{400} H_{310} N_{50} O_{120} SP + \text{or } 10 \bar{P}r + SP$ , which, as we shall presently see, is identical with the formula for fibrin.

The albumen of the blood differs from this, in containing one additional atom of sulphur; its formula is  $10 \bar{P}r + S_2 P$ .

Most of the chemical observations on protein apply equally to albumen, and therefore without entering into any description of the various chemical changes that occur upon the addition of reagents, we shall simply notice the physical appearances presented on the application of the ordinary tests.

Albumen is precipitated from its fluid solutions by all the ordinary acids, with the exception of acetic, tartaric, and phosphoric (tribasic) acids; which not only do not precipitate it, but check the ordinary precipitation induced by heat. It is precipitated from its solution in these acids by ferrocyanide and ferridcyanide of potassium, the former of which yields a white, and the latter a yellow, precipitate. These precipitates are soluble in alkalis but not in acids. When these two substances are used as tests, their action may be impeded by the presence of free soda or its carbonate; the addition

<sup>1</sup> See Appendix I, Note 7.



of a few drops of acetic acid is therefore always advisable in this case. Bichloride of mercury, and nitrate of the black oxide of mercury throw down whitish precipitates. Either of these tests will detect the presence of  $\frac{1}{20000}$  part of dry albumen. Precipitates of various colours and appearances are thrown down by sulphate of copper, nitrate of silver, the acetates of lead, protochloride of iron, alum, tannin, creosote, alcohol, &c.

The precipitates which the metallic salts throw down with albumen are usually mixtures of two distinct substances, one a compound of albumen with the acid, the other a compound of albumen with the metallic oxide; the former is usually somewhat soluble, the latter insoluble.

The alkalis and their carbonates form soluble compounds with albumen, and frequently require to be neutralized before the ordinary tests can be efficiently used.

The tests in most general use are heat, and nitric acid. When they both produce turbidity or a precipitate, the existence of albumen may be considered as proved.<sup>1</sup>

*Coagulated albumen.* Coagulated albumen may be obtained by submitting the white of egg or the serum of the blood to a temperature of from 160° to 180°; 167° according to Simon.

The coagulated mass must be then rubbed in a mortar, and successively digested in water, alcohol, and ether, until all substances soluble in those fluids are removed: it must then be carefully dried.

When obtained in this manner, it usually contains from 1 to 2% of phosphate of lime, an earth which soluble albumen seems to have the power of dissolving.

In order to obtain it free from this impurity, the following process may be employed. Coagulate albumen with dilute hydrochloric acid, wash the precipitate with water acidulated with the same acid, and then add so much cold water as may suffice to dissolve it. On the addition of carbonate of ammonia, coagulated albumen is separated as a flocculent, white precipitate. To remove any fat that may be present, it should be digested in hot alcohol or ether.

When dry, it is yellow and transparent; it swells upon being placed in water, but is only very slightly soluble in it. In its ordinary chemical relations it resembles protein.

<sup>1</sup> An apparent exception in the case of the urine will be subsequently noticed.



Albumen always contains more or less salts, phosphate and sulphate of lime, chloride of sodium, and probably some lactates. Their amount is variously estimated by different chemists: the average is about 4 to 8%.

In the albumen of the egg Mulder found 0.3%, and in that of blood, 0.4% of sulphate of lime.

The development of the young animal in the egg of the bird during incubation affords a striking illustration of the physiological import of this substance. It is easily shown that the egg contains no nitrogenous compound except albumen. The albumen of the yolk has been proved, by the analyses of Bence Jones and Scherer, to be identical with the albumen of the white; and in addition to this the yolk only contains a yellow fat with traces of iron. Yet we see in the process of incubation, during which no foreign matter, except atmospheric air, can be introduced, or can take any part in the development of the animal, that feathers, claws, blood-corpuscles, fibrin, cellular tissue, and vessels are produced.

*Diagnosis of albumen.* It coagulates at 167°. It is not precipitated by acetic or dilute sulphuric acid, and from these acid solutions it is precipitated by ferrocyanide of potassium. Corrosive sublimate and nitric acid throw down copious deposits.

### 3. *Fibrin.*

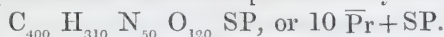
This modification of protein occurs in two forms, dissolved and coagulated. The former occurs in blood, lymph, chyle, juices of plants, &c., as long as these fluids form a part of the living organism; on their withdrawal from the influence of the vital force, the fibrin speedily coagulates. It is found in both these states in the animal and vegetable kingdoms.

The best method of obtaining it for chemical examination is either by briskly stirring newly-drawn blood with a little bundle of twigs, or else by shaking it in a stoppered bottle with a few bits of lead or tin. The fibrin adheres to these substances in the form of a nearly colourless coagulum. This must be washed in cold water till it ceases to give off any colour whatever; it must then be treated with boiling ether, in order to remove the fat which is always associated with it.

When dried, it assumes a pale yellow colour, is devoid of

taste and odour, and is insoluble in water, alcohol, and ether. When placed in water it sinks; it speedily absorbs a portion of the fluid, swells up, assumes its original bulk, and increases its weight threefold.

The composition of fibrin is represented by the formula<sup>1</sup>



The observations which have been made respecting the action of acids and alkalies on protein apply equally to fibrin.

Fibrin is stated to have the power of decomposing binoxide of hydrogen catalytically with the evolution of oxygen and heat. According to Scherer this action is induced by fresh fibrin from any source, but not by boiled fibrin. This power is not possessed by albumen.

A concentrated solution of nitrate of potash dissolves humid fibrin in the course of twenty-four hours, and gives it the properties of albumen. (Denis.) This observation requires further confirmation; it has failed in the hands of Simon and other chemists, and it is not impossible that the phenomena described by Denis were due to the presence of some uncombined potash.

The average quantity of fat associated with fibrin was found by Simon to vary from 2 to 4%, which agrees closely with the results of other observers.

Fibrin always contains a certain amount of salts, especially of the phosphate and sulphate of lime: the former seems to be chemically combined with it. The amount, according to Simon, lies between 1.5 and 2%.

*Diagnosis of fibrin.* Fibrin is distinguished by its spontaneous coagulation, by its insolubility in water, alcohol, and ether, and by its precipitation from acid solutions by ferrocyanide and ferridecyanide of potassium.

#### 4. Casein.

This substance constitutes the most important ingredient in the milk of the mammalia. We have already shown that it also exists in vegetables.

Casein may be obtained with facility by either of the following methods.

<sup>1</sup> See Appendix I, Note 8.

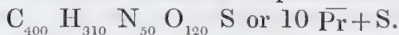
*a.* Evaporate milk to dryness in the water-bath ; triturate the solid residue and treat it with boiling ether, as long as it gives off any butter. When this ceases to be the case, remove the butter, and evaporate off the ether ; dissolve the residue in water, and filter. On the addition of alcohol to the clear filtered fluid, the casein is separated and thrown down. In order to remove any sugar of milk that may be entangled with the casein, the precipitate may be redissolved in water, and again thrown down by alcohol ; if it be now collected and dissolved in water, it affords a tolerably pure solution of casein.

*b.* Casein may also be obtained by the addition of sulphuric (or any other) acid. Sulphate of casein is precipitated, which must be carefully washed in water, freed in the ordinary manner from butter, &c. and then digested with carbonate of lime. By careful and, if necessary, repeated filtration we obtain a clear solution, which however is not free from lime.

A solution of casein prepared according to either of these methods is possessed of little flavour ; on the application of warmth it evolves a milky odour, and during evaporation it becomes covered with a skin or film, which on being removed is speedily renewed. This skin is due to the action of oxygen, for it does not form in an atmosphere of carbonic acid.

By a continuance of the evaporation we ultimately obtain a residue of dry casein. It appears as a brittle yellow substance. It does not admit of being perfectly dissolved in water, in consequence of a portion of it having assumed an insoluble condition during evaporation.

According to Mulder<sup>1</sup> casein is represented by the formula



The action of milk in the nutrition of young animals proves that casein is capable of being converted into albumen, and fibrin ; while the production of milk in an animal fed on albumen or fibrin shows that these substances may be reconverted into casein.

The alkalies exert a similar solvent power over casein as over protein and its other modifications. The metallic salts also form similar double compounds. It differs from albumen, in being precipitated by *all acids*. The latter reagents must be

<sup>1</sup> See Appendix I, Note 9.

applied cautiously, as casein is soluble in an excess of many acids.

On the addition of ferrocyanide or ferridcyanide of potassium to a perfectly neutral solution of casein, a slight precipitate is observed; if the solution is alkaline there is no perceptible effect, but if it is first rendered acid by a little acetic or dilute sulphuric acid, a copious precipitate is thrown down by both tests.

The casein of cow's milk is thoroughly precipitated by the mucous membrane of the calf's stomach; on the addition of this reagent to woman's milk, imperfect coagulation sometimes occurs; in other cases no apparent action is produced; the coagulation is never perfect. In this case the mucous membrane of the child's stomach produces a more energetic effect than that of the calf. If a quantity of potash or ammonia be added to the milk, sufficient to give it a decidedly alkaline reaction, no coagulation is effected.

Rochleder has recently attempted to show that pure casein is a substance nearly insoluble in water; that the so-called soluble casein is a combination of casein with potash, soda, or lime; and that the coagulation of the soluble casein by acids is nothing more than a separation of the casein, resulting from the combination of the acid with the base of the casein compound. In this manner, he explains how solutions of potash prevent coagulation, when added in very small quantity to milk, and why (especially in warm weather) very slight causes are able to produce a coagulation of the milk; as only the smallest quantity of lactic acid is required to be formed, in order to neutralize the minute traces of soda, which are able to retain in a state of solution an enormous quantity of casein.

Coagulated casein is found in the milk, constituting the walls of the butter-vesicles. For the purpose of chemical investigation, it is best obtained by the addition of anhydrous alcohol to a solution of casein. When dried, it is hard, yellow, and transparent. In its chemical relations it closely resembles coagulated albumen.

The amount of ash left after the incineration of casein seems to vary considerably. Mulder estimates it at 3.8%, and Simon at 7%, in the casein of cow's milk. In casein from the milk of woman, Simon estimated it at 5%. Rochleder, whose experiments were made under the direction of Liebig, found that pure



casein left only 0.3%. The ash contains phosphoric, carbonic, hydrochloric, and sulphuric acids, in combination with lime, and traces of magnesia and iron.

*Diagnosis of casein.* Casein may be distinguished from albumen by its not coagulating at 167°, and by the skin which forms on its surface during evaporation. It is precipitated by all dilute acids, and redissolves in an excess of the test. It is thrown down from its acid solutions by ferrocyanide and ferridecyanide of potassium. Casein of woman's milk is less perfectly thrown down by dilute sulphuric, lactic, and hydrochloric acids, than the casein of cow's milk.

Simon has obtained a modified form of casein from the crystalline lens,<sup>1</sup> from tubercle, pus, and saliva.

It may be recognized as casein by the diagnosis which has been given, but it differs from human casein in its thorough precipitation by all acids; and from the casein of human and cow's milk by its greater solubility in hot alcohol of 0.915—0.925.

The *globulin* of Berzelius, which together with *hæmatin* forms the blood-corpuscles, is considered by Simon as a peculiar form of casein. Very little is known regarding it, further than that it is a protein-compound. Mulder<sup>2</sup> represents it by the formula  $15 \bar{P}r + S$ .

It must not be confounded with Lecanu's *globulin*, which is merely impure hæmatin mingled with some albumen.

### *Pepsin, Ptyalin, Chondrin, Glutin, Pyin.*

5. *Pepsin.* This name (from  $\pi\epsilon\pi\sigma\iota\varsigma$ , digestion) was given by Schwann, to a substance which constitutes the most essential portion of the gastric juice. The following directions for the preparation of pepsin are taken from Vogel's essay on the subject; they correspond in nearly every respect, with the method which was given by Wasmann, who has the credit of first obtaining it in an isolated state. The glandular membrane of the fresh stomach of the hog, is separated, and after being cut into small pieces, is treated with cold distilled water; after twenty-four hours' immersion, the water is poured off, and a fresh quantity added. This operation is repeated for several days, until

<sup>1</sup> See Appendix I, Note 10.

<sup>2</sup> *Ib.* Note 11.

a putrid odour becomes perceptible. The aqueous infusion thus obtained is precipitated with acetate of lead, which causes a white flocculent deposit, containing the pepsin mixed with much albumen; this precipitate is diffused through the water, and must be decomposed by sulphuretted hydrogen. When the liquor is filtered, the solution contains pepsin and acetic acid, while coagulated albumen and sulphuret of lead remain on the filter. In order to obtain solid pepsin, the filtered liquid is evaporated to the consistence of a syrup, at a very moderate temperature (according to Wasmann, not higher than  $95^{\circ}$ ), and absolute alcohol is then added to it. After some time a whitish bulky precipitate is formed, which is to be dried by exposure to the air; it then constitutes a yellowish viscid mass of a peculiar animal odour, and a disagreeable taste. Pepsin thus obtained has an acid reaction, because it always contains a small quantity of acetic acid. This is most efficaciously removed by heating the pepsin for some hours in a salt-water bath; by which means a white powder, soluble in water and possessing no acid reaction, is obtained. The action of a high temperature injures the digestive power of pepsin, but does not affect its chemical composition.

From Vogel's analysis<sup>1</sup> of this substance, it appears that it may be very nearly represented by the formula  $C_{48} H_{32} N_8 O_{10}$ . On comparing this with Liebig's formula for protein, it appears that pepsin may be formed from protein by the subtraction of two atoms of water, and the addition of two atoms of nitrogen.

The most remarkable property of pepsin is the power which its aqueous solution, when slightly acidulated, possesses of dissolving the protein-compounds. A solution containing only  $\frac{1}{60000}$  part of pepsin, and slightly acidulated, will dissolve coagulated albumen in six or eight hours. This property is apparently destroyed by the alkalis.

Sulphuric, hydrochloric, and nitric acids, when added in very small quantity to a solution of pepsin, throw down white flocculi, which redissolve in an excess of the test: on the addition of still more acid the precipitate again occurs.

Acetic acid throws down a precipitate which redissolves in an excess of the test; no second precipitate is thrown down by the addition of more acetic acid.

<sup>1</sup> See Appendix I, Note 12.

Pepsin is thrown down from its aqueous solution by bichloride of mercury, acetate of lead, the sulphates of iron, sulphate of copper, and perchloride of tin. Ferrocyanide of potassium throws down no precipitate from an acidulated solution of pepsin.

Pepsin, which is precipitated from a concentrated aqueous solution by anhydrous alcohol, is said to lose its digestive power.

According to Liebig, pepsin as a distinct compound does not exist; he ascribes the solvent power of the gastric juice to the gradual decomposition of a matter dissolved from the membrane, aided by the oxygen introduced in the saliva. (Animal Chemistry, p. 109 et seq.)

*Diagnosis.* Pepsin is soluble in water, insoluble in absolute alcohol and ether; it is known by its precipitation by dilute acids, by the precipitate being redissolved in a slight excess of the test, and by the non-occurrence of a precipitate on the addition of ferrocyanide of potassium to the acid solution. It is further distinguished from albumen by its being precipitable by acetic and dilute hydrochloric acids.

6. *Ptyalin.* This term has been applied to a peculiar animal matter that exists in the saliva. The following is the best method of obtaining it. Fresh saliva must be neutralized with acetic acid, and then evaporated on the water-bath; the residue must be extracted first with alcohol,<sup>1</sup> and then with spirit. The ptyalin will remain undissolved amongst the protein-compounds, and must be extracted from them by the addition of water, in which it is readily soluble, and with which it forms a viscid fluid. The evaporation of this aqueous solution yields ptyalin free from all animal matters, but containing a trace of salts. When dry it is colourless, transparent, and brittle, devoid of odour, but with rather a sickly taste.

It is readily soluble in water, but is insoluble in alcohol and ether. It is precipitated from its aqueous solution by alcohol, but not by the mineral acids, metallic salts, acetic or tannic acid.

Our knowledge of this substance is by no means accurate; no analysis has ever been published, and there is no doubt that

<sup>1</sup> The term *spirit* is used to denote alcohol of spec. grav. .833, which contains about 85% of anhydrous alcohol; by alcohol, anhydrous alcohol of spec. grav. .792 is implied.

all the animal fluids yield an extract to water, which strongly resembles, if it be not altogether identical with, ptyalin.

*Diagnosis.* Ptyalin may be distinguished from the protein-compounds by its indifference to ferrocyanide of potassium; and from pepsin by its non-precipitation by dilute acids.

7. *Gelatin—Chondrin and Glutin.* Under the term gelatin we include the organic tissue of bone, cartilage, sinew, ligament, skin, cellular tissue, and serous membrane. All these substances dissolve by long continued boiling in water, and the solution on cooling assumes a consistent gelatinous mass. It is represented in various degrees of purity by glue, size, and isinglass. Gelatin does not exist *as gelatin* in the animal tissues, but is formed from them by the action of boiling water. Müller has shown that there are two (if not three) distinct forms of gelatin. To that which is obtained from the permanent cartilages, the cornea, fungous bones, &c. the term *chondrin* is given, while *glutin* includes those forms of gelatin which are obtained from skin, serous membrane, hoof, bone, tendon, fibrous and spongy cartilage, cartilage of bone, &c. As chondrin and glutin differ not only in the sources from which they are derived, but also in many of their chemical characters, we shall consider them separately.

*Chondrin* is most easily obtained by boiling any of the permanent cartilages, as for instance those of the ribs, larynx, or joints, for about twenty-four hours, in water: the solution must then be strained, in order to remove any coagulated matters, and allowed to gelatinize; it must then be dried at a low heat.

In this state it is hard and brittle, colourless and transparent. It sinks in cold water, and swells very much, without dissolving.

Scherer has deduced from his analyses the following formula<sup>1</sup> for chondrin,  $C_{48} H_{40} N_6 O_{20}$ , which corresponds numerically with  $\overline{Pr} + 4 HO + O_2$ .<sup>2</sup>

Its formula, according to Mulder, is  $C_{320} H_{260} N_{40} O_{140} S$ , or  $20 (C_{16} H_{13} N_2 O_7) + S$ . When burned it leaves about  $4\frac{1}{2}$  of phosphate of lime.

Chondrin is precipitated from its solution, and not redissolved in an excess of the test, by acetic acid, tannin, the neutral and basic

<sup>1</sup> See Appendix I, Note 13.

<sup>2</sup> Deduced from Liebig's formula.



acetates of lead, sulphate of iron, chlorine, iodine, and bromine. The following substances also give well-marked precipitates, which are, however, soluble in an excess of the test, alum, sulphate of copper, nitrate of silver, perchloride of iron, and nitrate of the protoxide of mercury. Creosote produces an immediate turbidity, and renders a solution of chondrin gelatinous in the course of twelve hours. Alcohol throws down chondrin from a concentrated solution, in the form of a white, viscid, and tenacious mass. Ferrocyanide and ferridecyanide of potassium throw down no precipitates when added to an acid solution of chondrin.

*Glutin* may be obtained in a state of purity from common glue, of which it forms the chief ingredient. On placing glue in cold water it absorbs moisture, and swells into a tremulous jelly, but does not dissolve. The cold water must be changed as long as it continues to take up anything from the glue. The glue, after undergoing this purification, must be heated till it is perfectly fluid, and then strained through a cloth or coarse filter. It gelatinizes on cooling, and when dried represents pure glutin. In its physical characters it is nearly identical with chondrin, but is usually rather more coloured. It is represented by the formula<sup>1</sup>  $C_{13} H_{10} N_2 O_5$ . (Mulder.) Scherer assigns to it the formula  $C_{96} H_{82} N_{15} O_{36}$ , which is numerically equal to  $2 \bar{P}r + 3 N H_3 + H O + 7 O$ , but recent investigations tend to show that this formula gives an excess of hydrogen. When burned, glutin leaves a slight ash, consisting chiefly of phosphate of lime. By long continued boiling, glutin loses its power of gelatinizing; in this state its ultimate composition may be represented by the formula  $C_{52} H_{41} N_8 O_{21}$  or  $4 (C_{13} H_{10} N_2 O_5) + H O$ . In other words, it appears to be changed into a compound, in which four equivalents of glutin are united with one of water. If a stream of chlorine be passed through a solution of glutin, a compound of chlorous acid and glutin is obtained, which is analogous in type with the preceding substance. It is represented by the formula  $4 (C_{13} H_{10} N_2 O_5) + Cl O_3$ . This is the compound referred to in the note to page 9.

The most important test for gelatin (either glutin or chondrin) is tannin, which will precipitate it when diluted 5000 times.

<sup>1</sup> See Appendix I, Note 14.

Three different compounds of glutin and tannic acid<sup>1</sup> have been discovered, and submitted to analysis; they are, however, individually of no particular importance in a physiological point of view. The extreme facility with which tannin precipitates gelatinous matters gives a clue to the medicinal action of astringent drugs on the human organism. They at once form insoluble compounds, (for tannin acts similarly on the protein-compounds,) and do not enter the blood; and this is the reason of their being comparatively innocuous. According to Mulder a less amount of tannin than is contained in one ounce of cinchona bark would, if conveyed directly into the blood, cause instantaneous death.

Acetic acid produces a slight turbidity, which speedily disappears on the addition of an excess of the test. Alum either produces no visible effect, or else throws down a very slight precipitate, which soon disappears, and the other salts, which have been mentioned as reagents for chondrin, yield no (or at most, very slight) precipitates with glutin. Alcohol and creosote act much the same as on chondrin, and no precipitate is occasioned by the ferrocyanide or ferridecyanide of potassium.

On boiling glutin in an excess of caustic alkali, till ammonia ceases to be developed, sugar of gelatin (glycicoll) and leucin are produced in the ratio of four parts of the former to one of the latter. In order to separate these substances, the alkaline solution must be saturated with sulphuric acid, evaporated to dryness, and the residue boiled with alcohol. The leucin being more soluble in alcohol than the glycicoll may be extracted from the evaporated alcoholic solution by cold alcohol; the glycicoll will remain in an impure condition in the residue.

On treating glutin with concentrated sulphuric acid a colourless fluid is obtained, which, after prolonged boiling and saturation with carbonate of lime, yields, in addition to certain uninvestigated compounds, leucin and glycicoll. This method is stated by Mulder to yield a less quantity of glycicoll, in proportion to leucin, than the former.

*Glycicoll* crystallizes in colourless prisms from a solution in alcohol, and in rhombs from a spirituous solution. These crystals possess a very sweet taste, are perfectly neutral, resemble cholesterin in their appearance, dissolve in 41.4 parts of water and in 931 of alcohol.

<sup>1</sup> It must be remembered that tannin and tannic acid are synonymous terms.

The composition of glycoll is represented by the formula<sup>1</sup>



It is worthy of remark that on subtracting an equivalent of grape or diabetic sugar from two equivalents of glycoll, we obtain the elements of two equivalents of urea:



*The origin of glutin* in the animal organism is still unknown.

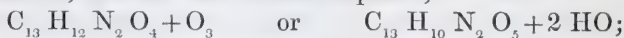
As no traces of it have ever been discovered in the vegetable kingdom, we cannot suppose that (like protein) it arises from that source. In all probability it is formed by the action of alkalis on protein; since we know that protein, submitted to such influences, yields products which in their chemical composition approximate closely to glutin, and that the blood is sufficiently alkaline to effect such, or similar, modifications.

In the hair, we find, associated with bisulphuret of protein  $\overline{Pr} + 2 S$ , a connecting tissue,  $C_{13} H_{10} N_3 O_5$ , which differs from glutin,  $C_{13} H_{10} N_2 O_5$ , simply by one atom of nitrogen.

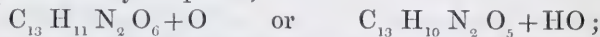
Moreover protid,  $C_{13} H_9 N O_4$ , and erythroprotid,  $C_{13} H_8 N O_5$ , nearly resemble glutin in their composition, and both glutin and the protein-compounds yield leucin when treated with caustic potash. These facts render it in the highest degree probable, that glutin is formed in the organism, from the decomposition of protein by alkalis; much as protid and erythroprotid are produced in the laboratory. A reference to the symbolical illustration in page 14, will show that with every two equivalents of ammonia that are developed, there are produced one equivalent of protid,  $C_{13} H_9 N O_4$ , and one of erythroprotid  $C_{13} H_8 N O_5$ . If we add to each of these the elements of one equivalent of ammonia, we obtain



It only remains for us to assume that the oxygen which is continually acting on the blood in the lungs, yields three equivalents of oxygen to the former, and one to the latter of these substances, and we have from the protid,



and from the erythroprotid,



that is to say, glutin and water may be supposed to be formed

<sup>1</sup> See Appendix I, Note 15.

from protid and erythroprotid by the ammonia, which the alkali of the blood evolves from the protein-compounds, with the cooperation of the oxygen of the atmosphere, in the lungs.<sup>1</sup> In the present state of organic chemistry, it is impossible in most cases, to state with certainty how changes such as these take place; we can only indicate the possible, and the most probable methods. That the gelatinous tissues are evolved from protein-compounds, in some manner or other, cannot admit of a doubt. From what other source can they be derived in the chick, but from the protein-compounds of the egg?

That chondrin and gluten, the two principal forms of gelatin, are closely allied to protein, is sufficiently clear. They will not however yield protein, when acted on by potash; neither do they produce a purple colour with hydrochloric acid. Consequently they do not contain protein. Hence it is that animals fed exclusively on gelatin, die with the symptoms of starvation, for the gelatin cannot yield albumen, fibrin, or casein; and the animal system, although it has the power of converting one protein-compound into another, does not possess the power of forming protein from substances which do not contain it. Consequently blood cannot be formed from gelatin, and the animal soon dies. The probable uses of a mixed gelatinous diet for convalescents, are pointed out by Liebig in his 'Animal Chemistry,' pp. 98-9.

*Diagnosis.* Chondrin and gluten may be recognized by their property of gelatinizing on cooling, and by the energetic action of tannin on their solutions. Ferrocyanide of potassium added to an acidulated solution of these substances, serves to distinguish them from the protein-compounds; and either acetic acid or alum will suffice to distinguish chondrin from gluten.

8. *Pyin.* This term was applied by Güterbock to a peculiar substance which occurs in pus, and which he isolates in the following manner. He precipitates the pyin, together with albumen, from pus, by the addition of strong alcohol. The

<sup>1</sup> The recent investigations of Enderlin, showing that there is no free alkali in the blood, but that its alkaline reaction is due to tribasic phosphate of soda, tend to throw considerable doubt on the ingenious hypothesis of Mulder, given in the text. It must also be remembered that leucin, protid, and erythroprotid have never yet been detected in the animal organism.



precipitate is treated with water, which dissolves the pyin : any albumen that may be dissolved at the same time, can be coagulated by heat, and removed by filtration ; and in this manner a tolerably pure solution of pyin is obtained. Vogel did not succeed in obtaining it ; and from Simon's researches it would hardly appear to be a constant constituent of pus, and purulent sediments.

Pyin is soluble in water and aqueous alcohol, but not in alcohol of .865, or stronger. It does not coagulate on boiling. When thoroughly dried it forms a gray powder, which does not admit of being perfectly redissolved in water. Acetic acid, tannin, and alum throw down precipitates, which are insoluble in an excess of the test. Ferrocyanide of potassium does not precipitate a solution of pure pyin ; but on the addition of a little hydrochloric acid, a precipitate appears, which immediately vanishes on the addition of a little more of the acid. According to Mulder, it is identical with tritoxide of protein.

*Diagnosis of pyin.* Pyin may be recognized by its reactions with acetic acid and alum. It may be distinguished from the protein-compounds (albumen, fibrin, casein,) in the same manner as pepsin and gluten. It differs from pepsin, by its acetic-acid precipitate not re-dissolving in an excess of the test, and from gluten and chondrin, by a similar behaviour on the part of the alum precipitate.

### 9. *Extractive Matters.*

After the removal of the protein-compounds from the animal fluids, there still remain certain salts, (lactates, chlorides, phosphates, and sulphates,) together with organic nitrogenous matter, which after evaporation remain as an amorphous mass. It is to this organic nitrogenous matter, after the salts have been removed by their appropriate solvents, that the term *extractive matter* is applied. It is as generally diffused over the whole system as the protein-compounds ; we meet with it in blood, bile, milk, urine, mucus, pus, and all the soft tissues, and most abundantly in muscular flesh. Hence the extractive matter of flesh merits especial attention. The extractive matters from other sources, as from blood, urine, milk, &c., will be subsequently noticed, and their leading characters contrasted with those of our standard extractive matter, the extract of flesh.

For the purpose of thoroughly examining the extract of flesh in all its chemical bearings, Simon experimented on eight pounds of the thickest part of a leg of pork, which he freed as much as possible from sinew, fat, cellular tissue, and everything that was not absolutely muscular flesh. It was then cut in small pieces, and cold water was poured over it. After being allowed to stand in water for some time, it was removed and boiled three successive times in fresh water. These boilings were collected, and a little fat skimmed off. The cold water in which it was first placed, was then boiled and mixed with the rest. The whole was then filtered, and appeared as a light yellow fluid, with a strong smell and taste of broth. This fluid was evaporated to the consistence of a thin syrup. After cooling, it did not gelatinize, and contained no gluten, or at most, a mere trace.

Alcohol was added to this thin syrup, until all the constituents insoluble in spirit, appeared to have separated, and deposited themselves at the bottom.

We thus separate the extractive matter into two distinct parts, one, soluble in water, but not in dilute alcohol, the other soluble in the latter menstruum.

The former, when evaporated at a gentle temperature is of a brownish yellow colour, and is tolerably firm, tenacious, and tough; it is termed *water-extract*.

The latter must be evaporated to the consistence of an extract, and treated with from twelve to sixteen times its volume of absolute alcohol. The mixture must then be heated, and well shaken, so as to mix the alcohol with the deposited portion as thoroughly as possible. The alcoholic solution clears on standing, and assumes a yellow colour. It must be removed from the insoluble residue, and gently evaporated to a clear brown syrup, which after cooling and standing for some time assumes a solid form; it dissolves freely both in water and absolute alcohol. By repeatedly treating the insoluble residue with hot absolute alcohol we remove all that is soluble in that fluid, and there is left a tolerably firm, tough, brown extract, which is soluble only in aqueous alcohol, and to which the term *spirit-extract* is given. We distinguish the portion which is soluble in absolute alcohol by the term *alcohol-extract*.

The extractive matter is thus separated into three distinct parts: these are—

A. That which is soluble in water, but not in dilute alcohol: *water-extract*.

B. That which is soluble in water and spirit, but not in anhydrous alcohol: *spirit-extract*.

C. That which is soluble in water, in spirit, and in anhydrous alcohol: *alcohol-extract*.

A. The water-extract contains:

*a. Constituents precipitable by tannic acid:*

(a) A matter not precipitable by neutral acetate of lead, but by basic acetate of lead and bichloride of mercury.

(b) A matter precipitable by neutral and basic acetates of lead, and by bichloride of mercury.

*β. Constituents not precipitable by tannic acid:*

(c) A gummy matter not precipitable by neutral acetate of lead, or bichloride of mercury, but by basic acetate of lead.

(d) A matter freely precipitable by basic acetate of lead, and very slightly by neutral acetate of lead, and bichloride of mercury.

(e) A matter precipitable by neutral and basic acetates of lead, but not by bichloride of mercury; the *Zomidin* of Berzelius.

B. The spirit-extract contains:

*a. Constituents precipitable by tannic acid:*

(a) A matter not precipitable by neutral or basic acetate of lead, but by bichloride of mercury.

(b) A matter not precipitable by neutral acetate of lead, or bichloride of mercury, but by basic acetate of lead.

(c) A matter precipitable by neutral and basic acetate of lead, but not by bichloride of mercury.

*β. Constituents not precipitable by tannic acid:*

(d) A matter rather indifferent towards reagents.

(e) A matter discovered and described by Chevreul; *Kreatin*.

C. The alcohol-extract contains :

a. *Constituents precipitable by tannic acid :*

(a) A matter precipitable by basic acetate of lead, and bichloride of mercury, but not by neutral acetate of lead.

(b) A matter precipitable by basic acetate of lead, and by an excess of bichloride of mercury, but not by neutral acetate of lead : it is crystalline.

β. *Constituents not precipitable by tannic acid :*

(c) A matter precipitable by basic acetate of lead, but not by neutral acetate of lead, or bichloride of mercury.

The substances Aa, Ab, Ba, &c., must be regarded as the proximate constituents of the three groups of extractive matters.

We shall arrange them in two classes, according as they are or are not precipitable by tannin.

*Constituents of the extract of flesh, precipitable by tannin.*

Aa exists in very small quantity in the water-extract : it may be distinguished from the protein-compounds by its indifference towards ferrocyanide of potassium ; from pepsin and pyin, by its indifference to dilute acids ; and from chondrin and glutin by its aqueous solution, not gelatinizing on cooling.

Ab may be distinguished in the same manner as Aa, from the protein-compounds, pepsin, &c.<sup>1</sup> It differs from Aa in being precipitated by protochloride of tin. When isolated it is tolerably soluble in alcohol, although that fluid will not extract it directly from the water-extract.

Ba occurs in minute quantity in the spirit-extract. It may be distinguished from the preceding compounds by its solubility in spirit, and by its reaction with the acetates of lead.

These three substances, Aa, Ab, and Ba, differ so slightly in their reactions with various tests, that we may conclude that in all probability they are merely modifications of one and the same matter.

<sup>1</sup> The same observation applies equally to all the following constituents of extractive matter.



*Bb* may be distinguished from the preceding compounds by its indifference towards bichloride of mercury.

*Bc* is freely precipitated by the addition of sulphate of copper, but the deposit which is of a brownish colour, readily dissolves in an excess of the test. If just a sufficient quantity of the solution of sulphate of copper to dissolve the precipitate be added, and heat applied, a green precipitate forms, and the supernatant fluid is likewise green. Alum, cautiously added, throws down a brownish yellow flocculent precipitate, which dissolves in an excess of the test. Infusion of galls, added in small quantity scarcely produces any turbidity in a solution of this constituent, but when added freely, a copious precipitate is deposited, which disappears on the application of heat, but returns as the solution cools. *Bc* may be distinguished from *Aa*, and *Ab*, by its indifference towards bichloride of mercury; from *Ba*, and *Bb*, by its behaviour with neutral acetate of lead, and sulphate of copper.

*Ca* is precipitable by protochloride of tin. This, together with the reactions it displays towards bichloride of mercury and infusion of galls, and its solubility in anhydrous alcohol, is sufficient to distinguish it from any of the preceding constituents.

The characteristics already mentioned are sufficient to distinguish *Cb*.

*Constituents of the extract of flesh not precipitable by tannin.*

*Ac* is remarkable for its indifference towards reagents. The only important tests have been already mentioned.

*Ad* is freely precipitated by bichloride of platinum; moreover the precipitate thrown down by basic acetate of lead is increased by heat.

*Ae* (*zomidin*) yields a very copious green or grayish green deposit, on the addition of acetate of copper. This precipitate does not dissolve in an excess of the test, but dissolves freely in acetic acid: on boiling this precipitate in caustic potash it is rendered brown, while the supernatant fluid assumes a faint purple red tint. Infusion of galls renders a solution of *zomidin* slightly turbid, and after some hours a few flocculi are deposited, possibly in consequence of the existence of some impurity in the *zomidin*.

Berzelius considers that the savour of boiled and roasted meat depends on this constituent.

Bd yields a yellow precipitate to bichloride of platinum, a white deposit to the acetates of lead, and its solution is rendered slightly turbid by infusion of galls: the turbidity however disappears on the application of heat.

Be (*kreatin*) is distinguished from all the preceding substances by its property of separating in rectangular crystals, and by its indifference towards the ordinary reagents.

Cc yields a copious white precipitate (which soon darkens) to nitrate of silver, and a chocolate-brown deposit to a solution of iodine.

There can be no doubt from the recent investigations of Mulder, that the binoxide and tritoxide of protein occur in the constituents of the water-extract, and are probably identical with some of them.

The relative proportions of water-, spirit-, and alcohol-extract in flesh, blood, urine, and milk, appear to fluctuate. Simon found that, in the extractive matter of flesh, the water-extract predominates, while he could only obtain a very small amount of spirit-extract; in the extractive matter of blood, the water-extract is also the most abundant, but here the amount of alcohol-extract is less than that of spirit-extract; in the extractive matter of urine, the water-extract was the most scanty, and the alcohol-extract the most abundant; and in the extractive matter of milk, the alcohol-extract was the least of the three.

*Extractive matter of blood.* Simon gives the following directions for the exhibition of the extractive matter of blood. A quart of blood is heated to the boiling point, and a sufficient quantity of water is then added to reduce it to a thin pulaceous state. After standing for some time, it is strained, and the red fluid which passes through is again boiled. In this manner we obtain a clear yellow fluid, which no longer becomes turbid on the application of heat. On evaporation, this fluid assumes a dark green colour; and on further concentration to the consistence of a syrup, it changes to a brown tint. At the same time a film forms on the surface, which leads to the conclusion that a caseous matter (in this case globulin) is present. The extract exhibits an alkaline reaction.

When the extract has been reduced to the consistence of a syrup, it is treated with alcohol of  $\cdot 833$ , which throws down a copious brown precipitate. The clear alcoholic fluid is removed and evaporated. It forms a brown extract, which is devoid of the aromatic odour that is perceptible in the spirit-, and alcohol-extract of flesh. The residue is evaporated to the consistence of a thin extract, and then treated with absolute alcohol, which, when evaporated, leaves a very small amount of alcohol-extract.

*Water-extract of blood.* It is of a dark brown colour, and possesses a strong taste of salt. Its reaction is slightly alkaline, and there is nothing remarkable about its odour. On incineration it leaves an alkaline ash, which effervesces on the addition of an acid.

The following are its most important chemical relations.

Acetic acid produces a turbidity which only disappears in a great excess of the test: ferrocyanide of potassium throws down a slight precipitate from the clear acid fluid, consisting of albumen.

Neutral and basic acetate of lead produce a copious brown precipitate; bichloride of mercury, even in excess, produces no apparent change. Infusion of galls induces merely a slight turbidity.

*Spirit-extract of blood* is of a dark brown colour, and a strongly salt taste. During evaporation it becomes covered with a coating of salts; and, after a certain degree of concentration, it solidifies, in consequence of the amount of the salts. It leaves a porous coal, which does not very easily burn to a white ash. This ash is strongly alkaline, and effervesces briskly on the addition of an acid.

The aqueous solution of the spirit-extract has a very feeble alkaline reaction.

Acetic acid produces a slight turbidity, which disappears on the addition of a considerable excess of the test.

Neutral and basic acetates of lead and infusion of galls produce copious precipitates; bichloride of mercury effects no apparent change.

*Alcohol-extract of blood.* When the alcohol in which this substance is contained is evaporated to the consistence of an extract, and then warmed with ether, we obtain a greenish brown matter, which, after the evaporation of the ether, is

soluble in water. Its amount is very minute ; it has a feeble, alkaline reaction, and possesses a very disagreeable and nauseous taste. It is precipitated by perchloride of tin and nitrate of silver, but not by neutral or basic acetate of lead, bichloride of mercury, or infusion of galls.

*Extractive matter of urine.* The urine must be evaporated in order to precipitate the salts as much as possible, and then placed in a freezing mixture for the same purpose. When it is reduced to the consistence of a thick syrup, alcohol of .833 must be added to it as long as any additional precipitate is thrown down. This precipitate consists of salts, and contains hardly any extractive matter ; it must be separated from the supernatant fluid, washed with alcohol of .833, dissolved in water, and precipitated again by alcohol. In this manner the spirituous solution assumes a yellow colour, while the salts are rendered colourless. By the evaporation of this yellow spirituous solution we obtain the *water-extract of urine*. It exists in very minute quantity. Infusion of galls produces hardly any marked effect, neither does bichloride of mercury ; neutral and basic acetates of lead yield a copious precipitate.

*Spirit-extract of urine* is obtained by evaporating the spirituous solution to the consistence of a thick extract ; it is then treated with a little anhydrous alcohol, and subsequently with ether. By shaking, and the application of a gentle warmth, the ether assumes a yellow colour, and a light brown matter separates ; this must be washed in ether, and then treated with absolute alcohol, which throws down a brown extractive matter, while the alcohol assumes a nearly similar tint. This precipitate must be washed with absolute alcohol, dissolved in water, and evaporated. Its ash contains a considerable amount of chlorides. Infusion of galls, bichloride of mercury, and neutral acetate of lead do not affect its solution, but basic acetate of lead throws down a copious precipitate.

*Alcohol-extract of urine* is obtained by the evaporation of the brown alcoholic solution referred to a few lines back. On the addition of anhydrous alcohol it is reduced to a yellow fluid, from which urea separates on slow evaporation. After the removal of this substance, we have the substance known as alcohol-extract of urine. Infusion of galls, bichloride of mer-



cury, and neutral acetate of lead do not influence its solution; it is, however, precipitated by basic acetate of lead.

*Extractive matter of milk.* For the purpose of investigating the properties of this substance, Simon evaporated a quart of woman's milk (partly colostrum and partly during the early weeks of lactation) to about eight ounces, and he then removed the casein and butter by the addition of alcohol. After filtration, some water was added; the fluid was again evaporated to a residue of a few ounces, treated with alcohol of .833, and allowed to rest for some time. Sugar of milk of a slightly yellow colour was deposited, and the supernatant fluid had nearly the same tint. The latter was evaporated on the water-bath to the consistence of a syrup, and then treated with anhydrous alcohol, which reduced nearly the whole syrup to a solid consistence, while the alcohol above it, which contained the alcohol-extract, was hardly tinged yellow. The precipitate which is thrown down by the anhydrous alcohol contains the spirit-extract, and the water-extract is contained in the yellow-coloured sugar of milk.

The *water-extract of milk* is obtained by treating the precipitated sugar of milk with water, and allowing it to stand, well covered, for some days. In this manner we obtain a yellow, almost clear, and viscid fluid, standing above the white sugar of milk. On removing this fluid, and allowing it to evaporate spontaneously, a fresh quantity of sugar of milk is deposited; in fact, it appears impossible to remove *all traces* of this constituent of the milk from the water-extract. Alcohol throws down a yellow, glutinous, tough extract, which exhibits a feeble alkaline reaction towards litmus paper. This is the water-extract. When burned, it leaves a porous coal, from which a white alkaline ash, containing carbonates, may be obtained without much difficulty.

It is precipitated from its solution by infusion of galls, basic and neutral acetates of lead, but not by bichloride of mercury.

The *spirit-extract of milk* is obtained from the precipitate which was thrown down by the anhydrous alcohol; it must be dissolved in a little water, and treated with alcohol of .833, which usually causes the separation of a little sugar of milk. The spirituous solution must now be evaporated to a very small residue, and some distilled water added, which produces

a considerable turbidity, and ultimately causes a slight white precipitate. The nature of this precipitate remains doubtful. The spirit-extract is thrown down from its solution by infusion of galls and basic and neutral acetates of lead, but not by bichloride of mercury.

The *alcohol-extract of milk* is obtained by the evaporation of the yellow anhydrous alcoholic solution that has been already referred to. It exists in very minute quantity, is of a yellow colour, and is not materially affected by infusion of galls, basic or neutral acetates of lead, or bichloride of mercury.

Ptyalin and pyin may be regarded as water-extracts of saliva and pus.

## 10. Colouring Matters.

### 1. THE BLOOD.

*a. Hematin.* This colouring matter is inclosed in thin sacs or vesicles, composed of a protein-compound, globulin: these vesicles exist in countless numbers in the circulating fluid, and are termed blood-corpuscles.

It has been generally assumed that this pigment exists in two distinct chemical states in arterial and venous blood, having in the former an excess of oxygen, in the latter an excess of carbon or carbonic acid. Mulder has, however, shown that its elementary composition is the same, whether obtained from arterial or from venous blood, and that it may be represented by the formula<sup>1</sup>  $C_{44}H_{22}N_3O_6Fe$ . Its composition seems likewise to be identical in all vertebrated animals.<sup>2</sup>

Various methods have been proposed for the exhibition of pure hæmatin. The following, adopted by Simon, is perhaps the simplest. Whipt and thoroughly dried blood must be pulverized, and its fat removed by repeated extraction with ether. It must then be boiled with anhydrous alcohol, and during the process of ebullition a quantity of sulphuric acid, diluted with cold alcohol, must be added, sufficient to communicate

<sup>1</sup> See Appendix I, Note 16.

<sup>2</sup> Lecanu examined hæmatin from human blood, and from that of the ox, domestic hen, duck, frog, carp, and mackerel. The only difference was in the proportion of peroxide of iron left when the hæmatin was incinerated.

a marked acid taste to the mixture. In this manner a blackish brown solution of sulphate of hæmatin is obtained, which must be saturated with carbonate of ammonia. If the mixture be allowed to stand for some time, the sulphate of ammonia may be separated by filtration; the greater part of the alcohol must then be removed by distillation. This part of the process requires much caution, and the distillation must be conducted very gently, as the action of the fluid is often violent. The hæmatin, which is ultimately precipitated, must be carefully washed with water, in order to remove any traces of sulphate of ammonia. It must then be dried on the water-bath, pulverized, and treated with ether as long as it continues to communicate a dark tint to that menstruum. The ether takes up a certain amount of hæmaphæin associated with fat. The hæmatin must be boiled in distilled water, as long as it continues to give off salts and alcohol-extract, and then in alcohol, till everything soluble in that fluid is removed. The substance that is left may be regarded as pure hæmatin.

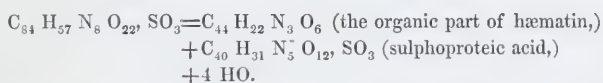
We can only isolate it in this coagulated and insoluble condition. In the blood-corpuscles it exists in a state of solution.

When obtained by the process that we have just described, it is of a blackish brown colour, is devoid of taste and odour, is insoluble in water, ether, fatty and ethereal oils, and in bisulphuret of carbon. It is usually stated to be insoluble in alcohol, but, according to Simon, boiling alcohol takes it up slightly. It is freely soluble in alcohol acidulated with sulphuric, hydrochloric, nitric, or acetic acid, and communicates a tint to that menstruum varying from a brown to a light red, according to the strength of the solution. On the addition of water the hæmatin gradually precipitates. Hæmatin dissolves freely in water or alcohol rendered alkaline by ammonia, potash, or soda: but the alkaline reaction is not in any degree neutralized by the hæmatin. On the application of a strong heat hæmatin swells up, gives off an animal odour, and burns with a clear flame. It leaves a voluminous coal, which is ultimately reduced to a dark red ash. When heated in a test tube it develops ammonia, and gives origin to a reddish empyreumatic oil.

Mulder has carefully examined the action of chlorine on hæmatin. He found that if a current of chlorine be transmitted through water containing hæmatin in suspension, the iron leaves

the other elements, and forms a chloride of iron, while the atom of metal thus removed is replaced by six atoms of chlorous acid, and a compound is formed, which is represented by the formula  $C_{44} H_{22} N_3 O_6 + 6 Cl O_3$ .

During this process the red colouring matter is destroyed, and the new compound appears as a white flocculent precipitate. It must not, however, be assumed from this experiment that the red colour of the blood is dependent on the iron, for that constituent may be removed from the hæmatin without materially affecting its tint, as may be shown in the following manner. Let some dried blood be mixed with concentrated sulphuric acid, and after standing for some days let water be added. Hydrogen gas is evolved by the action of the acid on the dried blood, and sulphate of the protoxide of iron is formed. If the blood, after this process, be carefully washed, a mixture of alcohol and sulphuric acid will extract from it red hæmatin in combination with sulphoproteic acid, but perfectly free from iron. Van Goudoever has deduced the following formula for this compound:



Although this experiment affords conclusive evidence that the red colour of the hæmatin is not dependent on the iron, yet this metal is very firmly combined with the four organic elements of this constituent. Well prepared hæmatin may be submitted for several days to the action of dilute hydrochloric or sulphuric acid, without the iron diminishing in the slightest degree.

Hæmatin treated in this manner, left after incineration 9·49% of peroxide of iron,<sup>1</sup> the amount that is always yielded by well-purified hæmatin.

			Peroxide of Iron.	Metallic Iron.
<sup>1</sup>	In 100 parts of hæmatin from human blood, Lecanu found	.	10·00	= 6·93
"	" from blood of ox	" "	12·85	= 8·90
"	" from arterial blood of ox, Mulder found,		9·60	= 6·66
"	" from venous blood of ox	" "	9·82	= 6·75
"	" from blood of ox, Simon found	.	11·50	= 7·97
"	" from blood of sheep, Mulder found	.	9·30	= 6·45



The condition in which the iron exists in hæmatin (whether as an oxide,<sup>1</sup> a carbonate, a carburet, or in the metallic state) has long been disputed.

The probability of its existence in a metallic state is strongly supported by the evolution of hydrogen that occurs when the clot is digested in sulphuric acid, and water is added; and Mulder suggests that this metal probably exists as an integral constituent of hæmatin, in just the same manner as iodine occurs in sponge, sulphur in cystin, or arsenic in the kakodyl series.

Numerous attempts have been made with the view to ascertain the proportions in which hæmatin and globulin combine, but the results have been very discordant. According to Berzelius, the hæmatoglobulin of human blood contains 100 parts of globulin, and 5·8 of hæmatin. Simon found the ratio to be 100 of globulin to 6·5 of hæmatin in the blood of a healthy young man, and 100 of globulin to 5·3 of hæmatin in the healthy blood of a stout girl. In disease, the variations are much greater. Simon has found as the limits 8·5 and 3·3 of hæmatin, corresponding to 100 of globulin.

Regarding the origin of hæmatin, it must clearly be generated in the organism, since it does not exist in the vegetable kingdom. Mulder conceives that it is generated from the normal constituents of the blood in the course of the circulation. Its destination also is obscure. In common with all the constituents of the body, it must be generated, consumed, and reproduced; but in respect to the actual metamorphoses that it undergoes in the organism, or their object, we are perfectly in the dark. Mulder suggests that the products of the decomposition of hæmatin may possibly be traced to the bilifulvin of the bile.

*Diagnosis.* Hæmatin may be known, both in its coagulated and soluble state, by its colour. When combined with globulin, in the blood-corpuscles, it may be recognized by the microscope. In its coagulated state it may be recognized by its insolubility in water, alcohol, and ether.

*b. Hemaphæin.* This term is applied by Simon to the brown colouring matter which seems to be associated with hæmatin in

<sup>1</sup> Iron is not separated from hæmatin by ammonia, potash, or soda; nor is its presence indicated by tannin or ferrocyanide of potassium, reagents which are so capable of detecting the presence of oxide of iron in ordinary cases.

the blood of the vertebrata, and is apparently identical, or nearly so, with the yellow colouring matter described by Sanson.<sup>1</sup>

It may be distinguished by its solubility in water, alcohol, and ether, and by the intense brown-red colour that it communicates to its alcoholic solution. When exposed to heat on a platinum spatula, it does not melt, but develops ammoniacal vapours, burns with a clear flame, and leaves a very trifling ash, which is perfectly free from peroxide of iron. Marchand remarks that hæmaphæin is nothing more than hæmatin modified by an alkali, just as O'Shaughnessy's *subrubrin*, and Golding Bird and Brett's *chlorohæmatin* and *xanthohæmatin* are products of the action of nitric acid on hæmatin.<sup>2</sup>

*c. Hæmacyanin*, or a blue colouring matter, has been detected by Sanson in healthy blood, by Lassaigne and Lecanu in the blood of icteric patients, and by Chevreul in the bile. Simon never succeeded in detecting it. For the method of isolating it, and for a description of its chemical characters we must refer to Sanson's paper. It is sufficient to remark that it is described as being insoluble in water, alcohol, and ether, but slightly soluble in boiling alcohol, from which, however, it separates on cooling. On the addition of ammonia to its alcoholic solution, a green colour is evolved, but on the addition of an acid, the blue colour is restored. It contains no iron.

## II. THE BILE.

*a.* The most important colouring matter of the bile is that to which it owes its characteristic brownish yellow tint. It is termed *cholepyrrhin* by Berzelius, and *biliphæin* by Simon. We shall adopt the latter term. On the gradual addition of nitric acid to a fluid that contains this substance in solution, a very characteristic series of tints are evolved. The fluid becomes first blue, then green, afterwards violet, and red, and ultimately assumes a yellow or yellowish brown colour.

<sup>1</sup> Journal de Pharmacie, Août 1835, p. 420.

<sup>2</sup> The discovery of the true nature of subrubrin is due to Drs. Brett and Golding Bird, who showed that it is merely hæmatin mixed with a little albumen. Their chlorohæmatin is hæmatin partly oxidised by nitric acid, as Marchand observes; and their xanthohæmatin is at present supposed by Dr. G. Bird to be identical with some of the products of the oxidation of protein recently described by Mulder.

All attempts to isolate this substance from the bile, by chemical means, have failed; it is apparently decomposed by the processes that are adopted in the analysis of this complicated fluid. We sometimes, however, find it deposited in the form of a yellow powder, in the gall-bladder, or concreted, with a little mucus, constituting a biliary calculus.

In this manner we have an opportunity of examining its chemical reactions. Biliphæin is of a bright reddish-yellow colour, and is only slightly soluble in most fluids; it is devoid of taste and odour, and yields ammonia on dry distillation. Water takes up an extremely minute trace of biliphæin, just sufficient to communicate a faint yellow tinge. Alcohol dissolves more than water, but only a very inconsiderable quantity. Its best solvent is a solution of caustic potash or soda, both of which are more efficient than ammonia. On exposing this solution to the atmosphere, oxygen is absorbed, and the yellow colour becomes gradually green. On the addition of an acid to this yellow or green solution, there is a precipitation of green flocculi which possess all the properties of chlorophyll, or the green colouring matter of leaves. In this state it is termed *biliverdin* by Berzelius. It is no longer biliphæin (or cholepyrrin), but a product of its metamorphosis.

The colouring matter of the bile may be separated from a composite animal fluid, by evaporation to dryness; by successive extractions with alcohol of .845, ether, and water; by dissolving the colouring matter in a solution of potash, and then precipitating it, as biliverdin, by hydrochloric acid.

*Diagnosis.* The action of nitric acid affords a certain test of the presence of biliphæin.

*b.* After the separation of the biliphæin, by conversion into biliverdin, another colouring matter remains, to which Berzelius has given the name of bilifulvin. It is a double salt of lime and soda, combined with an organic nitrogenous acid, to which the term bilifulvic acid has been applied. When isolated, this acid is insoluble in water and in alcohol, and separates in pale yellow flocculi when it is precipitated from an aqueous solution of its salts by a stronger acid. Whether bilifulvin is an actual constituent of the bile, or whether it is a mere product of metamorphosis, is unknown.

## III. THE URINE.

*a. Uroerthyrin.* In certain pathological conditions (especially in intermittent fevers) the urine possesses an intensely red colour, and deposits a dark red precipitate. Proust, who was the first that carefully examined this class of sediments, discovered in them a peculiar acid, to which he gave the name of *rosacic acid*. He subsequently found that this acid was merely a compound of uric acid with a red colouring matter. This red colouring matter has been observed by Landerer in the sweat from the axillary region of a girl with fever.

In order to isolate this pigment, we must boil a sediment of this nature in spirit, which will take up the colouring matter and a little uric acid. This uric acid must be removed by concentration and cooling, and then by evaporation to dryness, we obtain uroerythrin. It yields a vividly scarlet powder, is devoid of odour, possesses but little taste, and is tolerably soluble in water and spirit: these solutions are faintly acid.

*b.* The blue and black pigments that have been described by various authors (Braconnot,<sup>1</sup> Spangenberg,<sup>2</sup> Granier and Delens,<sup>3</sup> Marcet, Prout,<sup>4</sup> &c.) and have received the names of *cyanurin* and *melanurin*, are not of sufficient importance to require any observations.

11. *Bilin*.

*Bilin* is the name given by Berzelius to the substance which he considers as the principal and most important constituent of the bile.

The following is the most simple process for its exhibition:<sup>5</sup>

Acidulate perfectly fresh filtered ox-gall with a few drops of acetic acid, and precipitate it with neutral acetate of lead. The bilifellinic acid, which still remains in solution, must then be precipitated, as a plastery mass, by basic acetate of lead, and the filtered or decanted liquid, in which there is usually a little

<sup>1</sup> Ann. de Chem. et de Phys. t. xxix, p. 252.

<sup>2</sup> Schweigger's Journal, t. xlvii, p. 487.

<sup>3</sup> Ib. t. xxiii, p. 262.

<sup>4</sup> Medico-Chirurgical Transactions of London, v. xii.

<sup>5</sup> Lehmann, Lehrbuch der Physiologischen Chemie, t. i, p. 309.



bilifulvin, must be decomposed by an excess of carbonate of soda. The precipitate is then to be extracted with absolute alcohol, and the soda carefully precipitated from this solution by dilute sulphuric acid. On evaporating the alcoholic solution to dryness, we obtain *bilin*.

The composition of *bilin* is not accurately determined. It is easy to show that it contains nitrogen, by heating it with an alkali, in which case it develops ammonia. Lehmann always found traces of sulphur in it.

*Bilin* forms a gummy, pale yellow mass, which when quickly dried and pulverized, yields a white powder, devoid of odour and possessing a singular sweetish-bitter taste, most perceptible at the base of the tongue and on the posterior fauces. Berzelius suggests that the sweetness may be owing to the admixture of a little glycerin.<sup>1</sup> It is freely soluble in water and in alcohol, but not in ether; in fact it may be precipitated by ether from its alcoholic solution. When recently prepared, it is perfectly neutral. Heated to 212°, it begins to swell; at a higher temperature it becomes brown, develops a peculiar odour, and when inflamed, burns with a bright clear flame, leaving a porous ash.

An aqueous solution of *bilin* is not affected by acids, nor by earthy or metallic salts; neither does chlorine seem to induce any peculiar change. A concentrated solution of potash separates an oleaginous tough mass, (a compound of *bilin* and potash,) which is soluble in water and in alcohol.

*Bilin* is remarkable for the facility with which it undergoes metamorphoses. An aqueous or alcoholic solution *in vacuo* soon assumes an acid reaction. Its decomposition is accelerated by warmth, by the presence of organic matters, as mucus, &c., and more especially by the action of the mineral acids.

*Metamorphoses of Bilin. Bilin and hydrochloric acid.* On digesting *bilin* with dilute hydrochloric acid, five distinct substances are ultimately obtained, three of which are insoluble in water, and have received from Berzelius the names of *fellinic acid*, *cholinic acid*, and *dyslysin*; the remaining two being

<sup>1</sup> As the bile contains oleate, margarate, and stearate of soda, there is no difficulty in accounting for the presence of glycerin.

soluble in water, viz. *taurin* and hydrochlorate of ammonia. —The evaporation of an aqueous solution of the above mixture leaves as a residue a crystalline mass of taurin and hydrochlorate of ammonia; the latter may be removed by alcohol of 838, and the taurin may then be recrystallized from a solution in hot water.

*Taurin* forms colourless regular six-sided prisms, terminated by four- or six-sided pyramids. It is hard, crumbles between the teeth, has a cooling taste, but is neither bitter nor salt, dissolves in about sixteen times its weight of water at 60°, and is more soluble at a higher temperature. It is very slightly soluble in alcohol. It is dissolved without decomposition in concentrated sulphuric and nitric acids, and gives no reaction with the ordinary reagents. Its composition is represented by the formula  $C_4 N H_7 O_{10}$ . Hence, as Löwig remarks, it may be regarded as a combination of binoxalate of ammonia and water, for  $C_4 N H_7 O_{10} = 2 C_2 O_3 + N H_3 + 4 HO$ .

On treating the resinous mass, which is insoluble in water, with alcohol, *dyslysin* is left, and the two acids are dissolved. *Dyslysin* dissolves with some difficulty in boiling alcohol, and falls again on cooling as an earthy powder. It has not been further investigated.

*Cholinic* and *fellinic* acids are associated in the alcoholic solution. In many respects they closely resemble each other: they are almost insoluble in water, they dissolve in all proportions in alcohol, and they form nearly similar compounds with the alkalies, earths, and metallic oxides. Their salts of ammonia and baryta, however, differ in several respects, and by means of these reagents we can isolate the acids. If we evaporate a solution of their ammoniacal salts, choline of ammonia separates as a white soapy mass, while fellinate of ammonia remains in solution, and appears after due evaporation as a soft, greasy, yellowish substance.

When an aqueous solution of choline of ammonia is decomposed by hydrochloric acid, cholinic acid separates in light white flocculi, which after drying form a brown pulverizable mass. It is only slightly soluble in ether. The choline of baryta is almost insoluble in alcohol.

*Fellinic acid* may be exhibited in a similar manner. It separates from its solution in snow-white flocks, and after drying

forms a white, earthy, inodorous and bitter mass, which fuses at  $212^{\circ}$  without decomposition. In boiling water it undergoes fusion, and dissolves to a small extent; in this respect it differs from cholinic acid, which fuses but is wholly insoluble in hot water. It is soluble in ether, and its baryta salt dissolves freely in alcohol.

Fellinic and cholinic acids possess the property of combining and forming acid compounds with undecomposed bilin, to which Berzelius has given the names of *bilifellinic* and *bilicholinic acids*.

*Bilifellinic acid* apparently exists *as such* in fresh bile: it may be obtained either from bile after the removal of mucus, colouring matters, and other acids, by neutral acetate of lead, or from pure bilin.

In either case we add a solution of basic acetate of lead, which throws down a flocculent precipitate which soon collects into a soft, tenacious, plastery mass. The salt of lead must be decomposed by carbonate of soda, and the soda-salt in its turn, by sulphuric acid: we thus obtain a very soft, almost oily, yellow mass, from which the free sulphuric acid must be removed by carbonate of lead, and free fellinic and cholinic acids, by ether. We then obtain bilifellinic acid in the form of a thick syrupy fluid soluble in every proportion of water, and possessing a bitter taste. If this acid be digested with oxide of lead, or decomposed by basic acetate of lead, a plastery bilifellinate of lead is again precipitated, while at the same time pure bilin is found in the supernatant fluid. Hence it appears that bilin combines with fellinic acid in more than one proportion. *Bilicholinic acid* appears to resemble bilifellinic acid in almost every respect.

A mixture of these two bilin-containing acids constitutes Demarçay's *choleic acid*,<sup>1</sup> and forms the principal part of Thénard's biliary resin. (Berzelius.)

On cooling bilin in a solution of caustic potash till ammonia ceases to be developed, we obtain, on evaporation, a clotty matter, which, when dissolved in water and treated with acetic acid, precipitates a peculiar acid, the *cholic acid* of Gmelin. It forms fine silky acicular crystals, of which the taste

<sup>1</sup> This substance is described in the chapter on the Bile.

is at once sharp and sweet. It is slightly soluble in cold, but more so in hot water; it dissolves readily in alcohol: its solution reddens litmus. Most of the cholates are soluble, and possess a sweetish taste. Dumas assigns to this acid the formula<sup>1</sup>  $C_{42}H_{36}O_{10}$ .

There is no subject in the whole domain of animal chemistry that is more perplexing and intricate than the bile and its constituents. In the preceding pages we have adopted the views of Berzelius, but upon this point (cholic acid) he is very undecided. In the edition of his 'Animal Chemistry,' published in 1840, he states that he conceives it probable that cholic acid is produced by bilin alone, and that any fellinic or cholinic acids that may be simultaneously present take no part in the metamorphosis. In his article '*Bile*,' in Wagner's 'Handwörterbuch,' published two years later, he states that bilin in a state of purity undergoes only a very slight change by boiling with hydrated potash, and that he could not convert it into cholic acid in that manner. Cholic acid certainly does not pre-exist in the bile.

*Diagnosis of bilin.* Bilin may be detected by its peculiar taste. It is distinguished from the previous substances by its solubility in water and absolute alcohol, and by its insolubility in ether. Although absolutely pure bilin is said by Berzelius to be unaffected by metallic salts, basic acetate of lead and perchloride of iron throw down white precipitates from an aqueous solution; the latter, on the application of warmth, assumes a cinnamon tint: these reactions are probably owing to the presence of bilifellinic acid.

## 12. Urea.

Urea forms the principal constituent of the solid residue of normal human urine. It is found in considerable quantity in the blood after extirpation of the kidneys, also in certain pathological conditions in which the renal functions are not properly discharged, as in diabetes, cholera, ischuria, and Bright's disease. That it does exist in healthy blood as a constant, although *very minute* constituent, has also been recently proved by Marchand and Simon. Rees has detected

<sup>1</sup> See Appendix I, Note 17.



it in the liquor amnii and in milk ; Kühn and Lehmann in bile and biliary concretions ; Golding Bird in sweat ; Wright in saliva, MacLagan in the serous effusion into the ventricles in certain forms of fever ; and various chemists in dropsical fluids, &c.

Urea may be obtained from urine in a state of purity by any of the following methods.

*a.* The urine must be evaporated to the consistence of a syrup, and mixed when quite cold, with an equal volume of pure nitric acid of specific gravity 1.42. If the evaporation has been carried sufficiently far, the whole will form a thick crystalline mass, consisting of a compound of nitric acid and urea, which is sparingly soluble in nitric acid. All increase of temperature must be carefully avoided lest the nitric acid with the aid of heat, acting on the chlorides in the urine, should develop chlorine and nitrous acid, both of which, as we shall presently show, act powerfully in destroying urea. The impure crystals of nitrate of urea are to be carefully washed in dilute nitric acid, strongly pressed between folds of blotting paper, dried on a porous tile, redissolved in warm water, and neutralized with carbonate of lead. The residue after evaporation, must be treated with alcohol. In this manner we obtain an alcoholic solution of urea, from which sulphuretted hydrogen, and animal charcoal, will suffice to remove any traces of lead and colouring matter ; after due evaporation it will yield crystals of nearly pure urea.

*b.* O. Henry mixes the urine with basic acetate of lead, and then adds sufficient sulphuric acid to convert all the acetates into sulphates. After filtration through animal charcoal the fluid will yield on evaporation crystals of nearly pure urea.

*c.* Berzelius recommends that the alcohol-extract of urine should be dissolved in water, treated with animal charcoal, filtered, and warmed to about 120°, and that then as much oxalic acid should be added as the warm fluid will dissolve. Crystals form of sparingly soluble oxalate of urea, which must be dissolved, filtered through animal charcoal, recrystallized, and decomposed by carbonate of lime.

Urea may also be obtained artificially by the decomposition of certain cyanates. The following is the best method for obtaining it in this manner on a large scale. Twenty-eight parts of ferrocyanide of potassium, and 14 of peroxide of

manganese, are to be thoroughly mixed, and heated on an iron plate to a dull red heat. The mixture smoulders into a brown mass which contains cyanate of potash, carbonate of potash, and sesquioxide of manganese. When cold it is to be repeatedly digested in cold water, and the solution mixed with 20·5 parts of crystallized sulphate of ammonia dissolved in water. Sulphate of potash and cyanate of ammonia are formed; and this latter substance, on the application of a slight heat, is converted into urea. Sulphate of potash usually separates at once, in crystals; but, without stopping to remove them, we may evaporate the fluid on the water-bath to dryness, and remove the urea by a small quantity of water. On evaporating this aqueous solution to dryness, the urea may be extracted with boiling alcohol of 80 or 90%, whilst the sulphate of potash remains undissolved. The alcohol is allowed to evaporate, and the urea separates from it in crystals. In this manner a pound of ferrocyanide of potassium will furnish one third of a pound of pure urea.

The composition of urea is represented by the formula<sup>1</sup>  $C_2 H_4 N_2 O_2$ . It contains a larger proportion of nitrogen (46·728%) than any other organic compound.

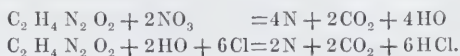
Urea when pure and in crystals is white and transparent: when deposited from a concentrated hot solution it is in the form of fine silky needles, but by very slow or spontaneous evaporation it separates in colourless flattened four-sided prisms of specific gravity 1·35. It is soluble in its own weight of cold, and in every proportion of hot water; in 4·5 parts of cold, and in 2 parts of boiling alcohol; it is slightly soluble in ether, about 1 part in 60, at a temperature of 62°.

It deliquesces in a very moist atmosphere only, and even then its chemical properties remain unchanged. In dry air it is perfectly permanent. It fuses at 250° into a colourless liquid, and is decomposed by a higher temperature into ammonia, cyanate of ammonia, and dry solid cyanuric acid. A concentrated watery solution may be boiled and preserved for a long time without any change, but if albumen, gluten, mucus, or especially ferment, should be present, it is speedily converted into carbonate of ammonia. The possibility of this transformation is obvious from the formula



<sup>1</sup> See Appendix I, Note 18.

With most concentrated acids it gives crystalline salts, especially with nitric and oxalic acids. It is not precipitated from its aqueous solution by metallic salts, ferrocyanide of potassium, or tannic acid. With hyponitrous acid it is instantly decomposed into nitrogen and carbonic acid gases, which are evolved in equal volumes; with chlorine it forms hydrochloric acid, nitrogen, and carbonic acid. These decompositions are rendered obvious by the formulæ



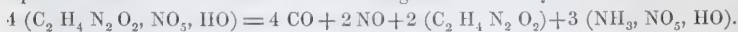
*Compounds of urea.* Nitrate of urea is obtained by the direct addition of nitric acid in excess, to a concentrated solution of urea. Its formula is  $\text{C}_2 \text{H}_4 \text{N}_2 \text{O}_2 + \text{NO}_5 + \text{HO}$ . It most commonly crystallizes in large colourless leaves, but sometimes in small solid prisms. It dissolves in eight parts of cold, but more freely in hot water. It is sparingly soluble in nitric acid, with which it may be boiled without decomposition. This salt effloresces with great rapidity.<sup>1</sup> 100 parts of nitrate of urea correspond to 48·945 of urea. (Regnault and Percy.)

*Oxalate of urea* is obtained by the mixture of concentrated hot solutions of urea and oxalic acid. Its formula is  $\text{C}_2 \text{H}_4 \text{N}_2 \text{O}_2 + \text{C}_2 \text{O}_3 + \text{HO}$ . It crystallizes in long slender plates or prisms, as the fluid cools, since it is much less soluble in cold than in hot water.

At a temperature of  $61^\circ$  water dissolves only  $4\cdot37\frac{0}{100}$ , and alcohol  $1\cdot6\frac{0}{100}$ , of the oxalate of urea. Oxalic acid displaces nitric acid from its combination with urea. 100 parts of oxalate of urea correspond to 62·564 of urea. (Berzelius.)

*Sulphate of urea* may be obtained by the double decomposition of oxalate of urea and sulphate of lime.

<sup>1</sup> Nitrate of urea, when heated to about  $316^\circ$ , decomposes, and disengages a considerable quantity of carbonic acid and nitrous oxide, in the exact proportion of two volumes of the first to one of the latter; the residue consists of free urea and of nitrate of ammonia. Nitrate of ammonia and urea crystallize successively out of an aqueous solution of the residue. These changes are shown by the formula



The nitrate of ammonia subsequently changes into water and nitrous oxide, and the urea into carbonic acid and ammonia.

During the decomposition of the nitrate of urea a new acid is formed in extremely minute quantities. It crystallizes in grayish white brilliant lamellæ, reddens litmus paper, and is very slightly soluble in water, which allows of its being separated from urea and nitrate of ammonia. Pelouze has assigned it the formula  $\text{C}_2 \text{H}_3 \text{N}_2 \text{O}_4$ .

*Hydrochlorate of urea* has been formed by the direct combination of dry urea with hydrochloric acid gas. It is a very unstable compound, and when exposed to the air dissolves into a very acid liquid, from which hydrochloric acid is disengaged.

*Lactate, hippurate, and urate of urea* have been described by Cap and Henry; who in fact assert that in human urine the urea exists as a lactate. Pelouze has, however, disproved the existence of all these compounds.

Prout has examined certain compounds of silver and lead, in which the urea seems to combine with the oxides of those metals as bases. They are of no importance in a practical point of view.

The presence of urea modifies the solubility and crystalline form of certain salts; it causes common salt to crystallize in octohedra, instead of in cubes; but it has been observed that if these octohedra are dissolved in pure water they recrystallize in cubes. This peculiarity affords a common microscopic test for the presence of urea.

*Diagnosis of urea.* Urea is distinguished by its solubility in water and in alcohol, and by its behaviour with nitric and oxalic acids.

### 13. *Uric acid.*

Uric acid is a constituent of the urinary secretion in apparently all classes of animals; it is found in man and the carnivora, in graminivora (Fownes),<sup>1</sup> in birds, amphibia, serpents, insects, and mollusca. It is the most common ingredient (in combination with a base) of urinary calculi and gouty concretions; it has been detected in the saliva (Wright), in sweat (Wolf),<sup>2</sup> and on the surface of ulcers in arthritic persons (Schönlein.)

Uric acid may be obtained in a state of purity, by the following process, from the excrement of the boa constrictor,<sup>3</sup>

<sup>1</sup> London and Edinburgh Phil. Mag. xxi, p. 139.

<sup>2</sup> Dissertatio sist. casum Calculositatis; Tubing. 1817.

<sup>3</sup> The excrements of the boa constrictor have been found by Prout to yield more than 90% of uric acid. (Annals of Philosophy, t. v, p. 413.) The excrements of the rattlesnake have been examined by Simon. He found in 100 parts of the dried residue—free uric acid, with a little fat and extractive matters, 56.4; urate of ammonia, 31.1; urate of soda, with some chloride of sodium, 9.8; urate of lime, 1.4; phosphate of lime, 1.3. Although we have retained the term "excrements" in accordance with popular usage, the substance is in reality the urine of the serpent.



which contains a very large proportion of uric acid and urate of ammonia. To powdered *boa constrictor's* excrement add an *equivalent proportion*, or slight excess, of caustic potash. (We assume that the excrement is entirely urate of ammonia in this calculation.) Boil in water (in the proportion of 1lb. of excrement to 2 quarts of water) till the mass is reduced to diffused gelatinous floccules, which speedily settle, leaving a dark-brown supernatant fluid. Remove this fluid by decantation or filtration, and wash the urate of potash, which is collected, with cold water. It must then be heated in water, and more caustic potash must be added, till the solution becomes clear. While still hot it must be poured into dilute hydrochloric acid, and allowed to stand. In this manner pure crystals of uric acid will be obtained.<sup>1</sup> The slight excess of caustic potash used in the first instance seems to keep the colouring matter in solution.

Uric acid is represented by the empirical formula<sup>2</sup>  $C_5 H_2 N_2 O_3$ , or  $C_{10} H_4 N_4 O_6$ , or  $C_{10} H_4 N_4 O_6$ ; it is highly probable that it contains one atom of water in this state, and may be considered as a hydrate,  $C_{10} H_4 N_4 O_5 + HO$ .

Uric acid crystallizes in fine scales of a brilliant white colour and silky lustre, is tasteless, inodorous, heavier than water, almost insoluble in cold, and very slightly soluble in boiling water.<sup>3</sup> It is insoluble in alcohol and ether. It dissolves in dilute nitric acid, with the evolution of equal volumes of carbonic acid and nitrogen: on evaporating the solution a pink tint is produced, which, on the addition of ammonia in excess, changes to a purple-red colour. This is a characteristic test of the presence of uric acid. Boiled with peroxide of lead in water it is decomposed into oxalic acid and allantoin, and urea is separated.

Several of the compounds of uric acid, with the alkalies and alkaline earths, are of practical importance.

*Urate of potash* is a frequent constituent of urinary calculi: it may be obtained by boiling urate of ammonia with potash. On cooling, the urate of potash yields a mass of very minute aci-

<sup>1</sup> The various forms under which uric acid crystallizes are noticed under the head of *Urinary sediments*.

<sup>2</sup> See Appendix I, Note 19.

<sup>3</sup> According to Liebig, uric acid requires 15,000 parts of cold, and 1,932 parts of boiling water, for its perfect solution. It dissolves in all alkaline fluids, in solution of phosphate of soda and of borax, but not in solutions of the bicarbonates of potash or of ammonia.

cular crystals, or else separates in granules or scales. It dissolves in 140 parts of cold, and in 85 parts of boiling water.

*Urate of soda* may be obtained in a similar manner, or by boiling uric acid in a solution of borax. It is far less soluble than the former salt; one part of it requiring for its solution 372 parts of cold, and 124 parts of boiling water. In other respects it closely resembles it. It occasionally constitutes a very peculiar stellar form of deposit in the urine. Liebig has shown that uric acid dissolves with great facility in a solution of common phosphate of soda, that the fluid from being alkaline becomes acid, and that there are formed a urate of soda, and an acid phosphate of soda. It is in this condition that he supposes uric acid to exist in the urine.

*Urate of ammonia*, in a state of purity, invariably crystallizes in needles, but if a little chloride of sodium be added to its solution we no longer obtain, on evaporation, a crystalline acicular deposit, but the peculiar amorphous form in which urate of ammonia occurs in urine. On the addition of chloride of sodium to water, in the proportion of 2.59 to 1000, the solubility of urate of ammonia is increased in the proportion of 1000 to 450, or is more than doubled. (Dr. Bence Jones, in Trans. of the Medico-chirurgical Society, 1844.)

According to Liebig, this salt requires for its solution 1727 parts of cold, and 243 parts of boiling water.

*Urate of magnesia* may be obtained by the addition of sulphate of magnesia to a boiling saturated solution of urate of potash. On cooling, and after the fluid has been allowed to stand for some time, urate of magnesia is deposited in fine needles of a silky lustre, and arrayed in stellar groups. At  $212^{\circ}$  these crystals lose 5 atoms of water. Urate of magnesia dissolves in 3593 parts of cold, and 263 parts of boiling water.

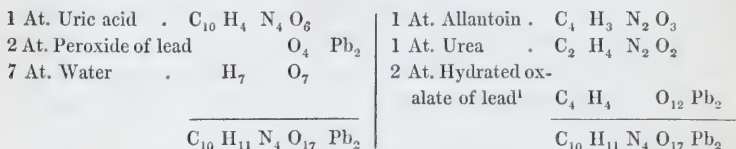
*Urate of lime* forms white glittering needles or leaves, which dissolve pretty readily in hot water, but are thrown down again on cooling.

*Diagnosis of uric acid.* Uric acid is distinguished by the form of its crystals under the microscope, by its insolubility in water and in alcohol, and by its behaviour towards nitric acid and ammonia.

*The Metamorphoses of Uric Acid. Allantoin.* One part of uric acid is boiled in 20 parts of water, and freshly prepared

peroxide of lead is gradually added to the boiling liquid, as long as its colour is observed to change. The hot liquid is then filtered and evaporated till crystals begin to form on its surface; on cooling they form in considerable quantity, and constitute *allantoin* or *allantoic acid*, while urea remains in the mother liquid, and oxalate of lead on the filter.

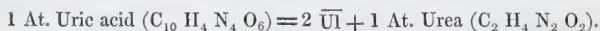
The following symbolical representation may elucidate this decomposition.



It is on this reaction that Liebig finds his theory of uric acid. He considers it to contain ready-formed urea and a hypothetical substance, for which he proposes the term *uril*  $\overline{U}$ , or cyan-oxalic acid.<sup>2</sup>

For 1 At. Uric acid ( $C_{10} H_4 N_4 O_6$ )—1 At. Urea ( $C_2 H_4 N_2 O_2$ ) = 2 ( $C_4 NO_2$ ) = 2  $\overline{U}$ .

Hence the rational formula for uric acid appears to be—



In the production of allantoin from uric acid, the urea is supposed to be set free, whilst the uril combines with oxygen and water in order to form oxalic acid and allantoin. The change may be illustrated in the following manner:  $2\overline{U} = C_8 N_2 O_4 = C_4 O_4 + C_4 N_2$ .

By the addition of 2 at. oxygen to the former term,  $C_4 O_4$ , we obtain  $2C_2 O_3$  (oxalic acid), and by the addition of 3 at. water to the latter,  $C_4 N_2$ , we obtain  $C_4 H_3 N_2 O_3$  (allantoin.)

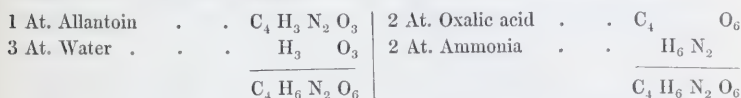
This substance *allantoin*, or as it is frequently termed *allantoic acid*, occurs ready formed in the allantoic fluid of the calf, from which it crystallizes spontaneously on cooling, when the fluid has been evaporated to one fourth of its volume. It then requires to be purified by recrystallization.

The crystals are colourless and transparent, tasteless and

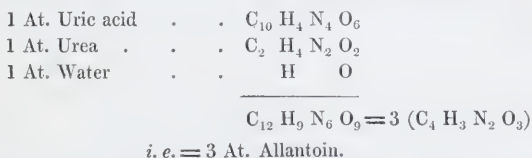
<sup>1</sup> 2 At. Hydrated oxalate of lead = 2 ( $Pb O, C_2 O_3, 2 HO$ )  
 $= C_4 H_4 O_{12} Pb_2$

<sup>2</sup> This name is suggested by its constitution; for 1 at.  $\overline{U} = C_4 NO_2 = C_2 O_2, Cy$ , a formula that represents oxalic acid in which an equivalent of oxygen is replaced by one of cyanogen.

inodorous, and exert no action on vegetable colours. They are usually prisms of the right rhomboid system, have a glassy lustre, and at  $68^{\circ}$  are soluble in 160 times their weight of cold, but in a much less quantity of hot water: they dissolve in hot alcohol, but recrystallize as it cools. At a high temperature allantoin is converted by the caustic alkalis, and also by most concentrated acids (with the exception of nitric acid) into ammonia and oxalic acid. This change may be illustrated by the formula



If we compare the composition of allantoin with that of uric acid and urea, we find that these substances bear a highly interesting relation to each other; if we add to one atom of uric acid, one atom of urea and one atom of water, we obtain a formula exactly corresponding with that of allantoin.



“According to this,” as Liebig observes, “it is evident that the product of the secretion of the non-respiring fœtus of the cow is, in a certain sense, identical with the products secreted by the kidneys of the breathing animals. Urea represents carbonate of ammonia from which the elements of two atoms of water have separated; allantoin represents oxalate of ammonia, from which the elements of three atoms of water have separated.”

We now proceed to the consideration of a few of the most important products of nitric acid with uric acid.

*Alloxan.* One part of dry uric acid is gradually added to four parts of nitric acid of spec. grav. 1.42—1.5, by which it is dissolved with effervescence, and the production of heat. The whole liquid is soon converted into a solid crystalline mass of *alloxan*. Its formula is  $C_8 H_4 N_2 O_{10}$ . It is very soluble in water, reddens vegetable colours, and causes a purple stain on the skin. Its formation may be explained in the following manner. We have already shown (see *Urea*,) that urea is con-



verted by hyponitrous acid into water, carbonic acid, and nitrogen. Hence, if we suppose that the 2 atoms of uril (bearing in mind that uric acid =  $2\overline{\text{U}}\text{I} + 1$  at. urea,) take up the 2 at. of oxygen, which the nitric acid has given off in the formation of hyponitrous acid, and 4 at. of water, we obtain the formula of alloxan, for



*Parabanic acid* is obtained by treating one part of uric acid, or one part of alloxan in eight parts of nitric acid, evaporating to the consistence of a syrup, and allowing it to stand for some time, when it yields colourless crystals which may be purified by recrystallization. Its formula is  $\text{C}_6 \text{N}_2 \text{O}_4 + 2\text{HO}$ .

It is formed by the action of hyponitrous acid on the urea of the uric acid; the 2 at. of uril take up 4 at. of oxygen, and 2 at. of water, and yield 2 at. of carbonic acid, and 1 at. of hydrated parabanic acid: thus



Or it may be regarded as produced by the action of oxygen on alloxan, for



*Oxaluric acid* is obtained by boiling parabanic acid in a solution of ammonia. If the mixture be evaporated and allowed to cool, crystals of oxalurate of ammonia will separate themselves. On the addition of an acid to a concentrated solution of this salt, oxaluric acid is separated as a crystalline powder. Its formula is  $\text{C}_6 \text{H}_3 \text{N}_2 \text{O}_7 + \text{HO}$ . It is formed by the addition of 2 at. of water to the constituents of parabanic acid: it contains further the elements of 2 at. of oxalic acid, and 1 at. of urea, and by boiling in water is completely decomposed into free oxalic acid, and oxalate of urea.

Liebig observes that "when uric acid is subjected to the action of oxygen, it is first resolved into alloxan and urea; a new supply of oxygen acting on the alloxan causes it to resolve itself either into oxalic acid and urea, or into oxaluric and parabanic acids, or into carbonic acid and urea," (*Animal Chemistry*, p. 137.) The reactions which we have already given are sufficient to explain this statement. We have shown that—

Uric acid =  $2\overline{\text{U}}\text{I} + \text{urea}$ , and alloxan =  $2\overline{\text{U}}\text{I} + \text{O}_2 + 4 \text{HO}$ ;  
consequently,



Moreover,

Alloxan = urea +  $C_6 O_8$  (see their respective formulæ);

therefore,

Alloxan + O = urea +  $C_6 O_9$  = urea + 3 at. oxalic acid,

and

Alloxan +  $O_4$  = urea +  $C_6 O_{12}$  = urea + 6 at. carbonic acid.

Also,

Alloxan +  $O_2$  = parabanic acid + 2 HO + 2  $CO_2$   
= oxaluric acid + 2 at. carbonic acid.

Hence,

Uric acid + 4 HO +  $O_3$  = 2 at. urea + 3 at. oxalic acid.

Uric acid + 2 HO +  $O_4$  = 2 at. urea + parabanic acid + 2 at. carbonic acid.

Uric acid + 4 HO +  $O_4$  = 2 at. urea + oxaluric acid + 2 at. carbonic acid.

Uric acid + 4 HO +  $O_6$  = 2 at. urea + 6 at. carbonic acid.

These formulæ express laws of much importance in urinary pathology; they show us that if an abundant supply of oxygen be given to the uric acid, carbonic acid and urea may be obtained; if a smaller quantity, oxalic acid and urea; and if none be given the acid remains unchanged.

*Murexid (Purpurate of ammonia.)* The best method of exhibiting this substance is to evaporate a solution of uric acid in dilute nitric acid, until it acquires a flesh-red colour: after it has cooled to  $160^\circ$  a dilute solution of ammonia must be added, till the presence of free ammonia is remarked by the odour. The solution is then to be diluted with half its volume of boiling water and allowed to cool: it crystallizes in short four-sided prisms, two faces of which reflect a green metallic lustre. It is insoluble in alcohol; sparingly soluble in cold, but more readily in boiling water, on the cooling of which it crystallizes unchanged. It is soluble in caustic potash with a beautiful indigo-blue colour, which disappears with the evolution of ammonia on the application of heat. The difference between the views of Prout and Liebig regarding this substance is, that the latter considers it a distinct principle, while the former regards it as a combination of a peculiar acid (purpuric) with ammonia. Prout's view has been strongly confirmed by the researches of Fritzsche, which are published in the Transactions of the Academy of Sciences of St. Petersburg, for 1839.

The formula assigned to this substance by Liebig and Wöhler is  $C_{12} H_6 N_5 O_8$ . Fritzsche gives it the formula  $C_{16} H_3 N_6 O_{11}$ , or  $C_{16} H_4 N_3 O_{10} + NH_4 O$ .

*Murexan or purpuric acid* is prepared by dissolving murexid in caustic potash by the aid of heat, which is to be applied till

the blue colour disappears: dilute sulphuric acid is then to be added in excess. It falls in crystalline scales of a silky lustre; is insoluble in water and dilute acids, but is taken up by ammonia and the fixed alkalies.

If a solution of murexan in ammonia be exposed to the air, it acquires a purple-red colour and deposits crystals of murexid: with an excess of ammonia it again becomes colourless, and is then found to contain oxalurate of ammonia.

Its formula, according to Liebig and Wöhler, is  $C_6 H_4 N_2 O_5$ ; according to Fritzsche it is  $C_{16} H_4 N_5 O_{10}$ .

The substances which have been described are only a few of the products of nitric acid on uric acid; they have been selected as having a more practical bearing than the others. The following table exhibits the principal results of Liebig and Wöhler's admirable paper on this subject.

- (a) On treating uric acid with cold concentrated nitric acid, we obtain *alloxan*,  $C_8 H_4 N_2 O_{10}$  or  $2\bar{U}I + O_2 + 4HO$ .
- (b) On treating uric acid with cold dilute nitric acid, we obtain *alloxantin*,  $C_8 H_5 N_2 O_{10}$ , or  $2\bar{U}I + O + 5HO$ .
- (c) On treating alloxan with sulphurous acid, we obtain *thionuric acid*,  $C_8 H_7 N_3 O_{14} S_2$ .
- (d) On treating thionuric acid, or thionurate of ammonia, with hydrochloric, or sulphuric acid, we obtain *uramil*,  $C_8 H_5 N_3 O_6$ , or  $2\bar{U}I + NH_3 + 2HO$ .
- (e) On treating alloxan with sulphuretted hydrogen, we obtain first, alloxantin, and subsequently *dialuric acid*,  $C_8 H_1 N_2 O_8$ , or  $2\bar{U}I + 4HO$ .
- (f) On warming uric acid in eight parts of nitric acid we obtain *parabanic acid*,  $C_6 N_2 O_4 + 2HO$ .
- (g) On boiling parabanic acid in ammonia, *oxalurate of ammonia* is generated, from which we can obtain *oxaluric acid*,  $C_6 N_2 H_3 O_7 + HO$ .
- (h) On the addition of an alkali to a concentrated solution of alloxan, we obtain *alloxanic acid*,  $C_8 H_2 N_2 O_8 + 2HO$ .
- (i) By the precipitation of a solution of alloxan with boiling acetate of lead, we obtain *mesoxalic acid*,  $C_3 O_4$ .
- (j) By heating a solution of alloxan with ammonia, we obtain *mycomelinic acid*,  $C_8 H_5 N_4 O_5$ .
- (k) On heating uramil with dilute sulphuric acid, we obtain *uramilic acid*,  $C_{16} H_{10} N_5 O_{15}$ .

- (l) On warming uric acid with nitric acid and saturating it with ammonia, we obtain *murexid*,  $C_{12} H_6 N_5 O_8$ .
- (m) On dissolving murexid in caustic potash and adding dilute sulphuric acid, we obtain *murexan*,  $C_6 H_4 N_2 O_5$ .

#### 14. *Hippuric Acid.*

*Hippuric*, or *urobenzoic acid*, is an ordinary, although not a constant, ingredient of the urine of the graminivora. It has been observed by Lehmann, Ambrosiani, and Reich, in the urine of diabetic patients, and Bouchardat has found it in the same secretion in certain anomalous cases to which he has applied the term "hippuric." Liebig has recently asserted that it is a constant ingredient of healthy human urine; and even if this statement be too general, there can be no doubt that it does very frequently occur in minute quantity in this secretion.

Hippuric acid is readily obtained by evaporating the urine of the horse or cow to about one tenth of its volume, and adding sufficient hydrochloric acid to give it a decidedly acid reaction. Yellow or brown crystals of hippuric acid are almost immediately deposited, which must be collected, dissolved in a hot solution of carbonate of soda, and filtered through animal charcoal. By the addition of hydrochloric acid to this solution, (which must be concentrated, if requisite,) we obtain tolerably pure crystals of hippuric acid.

This acid forms long transparent four-sided prisms, acuminate at the extremities; it is destitute of odour, and has a faintly bitter, but not an acid taste. It dissolves in about 400 parts of cold water, and in a much larger proportion in hot water, from which it recrystallizes on cooling. It is freely soluble in alcohol, less so in ether. A cold aqueous solution strongly reddens litmus. At a moderate heat, hippuric acid melts (without yielding water) into a colourless oily fluid, which, on cooling, solidifies into a crystalline milk-white mass. At a higher temperature the acid undergoes decomposition, and yields a crystalline sublimate composed of benzoic acid and benzoate of ammonia, while, at the same time, some red oily drops are produced, which develop a peculiar odour, resembling that of the Tonquin bean. Hydrocyanic acid is subsequently formed, and the previous odour is replaced by a bitter-almond smell. The action of perchloride of iron on this acid is worthy of notice. On the addition of this reagent to a solution of hip-



puric acid, a well-marked yellow colour is produced; no such change is effected on the addition of this test to a solution of uric acid. On its addition to a solution of hippurate of potash, a copious orange-coloured deposit is thrown down, which, on the application of heat, forms a red resinous mass, soluble in alcohol, but insoluble in water; when added to a solution of urate of potash, a precipitate is likewise thrown down, which is at first of a brownish red colour, but rapidly becomes yellow.

The composition of this acid is represented by the formula<sup>1</sup>  $C_{18}H_8NO_5 + HO$ . In its physical characters it strongly resembles benzoic acid, and there can be no doubt that these two acids have been often confounded: there is, moreover, a close analogy between them. They both belong to the benzoyl series, although the exact place of hippuric acid cannot be at present assigned to it with certainty. Oxidising agents (as nitric acid, or sulphuric acid and binoxide of manganese) convert hippuric into benzoic acid; and a similar change occurs in the urine if it be kept for any time. Conversely, benzoic and cinnamic acids are converted in the organism into hippuric acid.<sup>2</sup>

Hippuric acid forms soluble crystallizable salts with the alkalies and alkaline earths.

*Diagnosis.* Hippuric acid may be distinguished by its crystalline form, its solubility in alcohol, its behaviour when heated, and its reaction with perchloride of iron. Nitric acid will suffice to distinguish it from uric acid.

### 15. *Uric Oxide.*

*Uric oxide, xanthic oxide, urous acid.* This substance is a very rare ingredient in vesical calculi. It was discovered by Marec, who gave it the name *xanthic oxide*; it has since been met with by Laugier, Stromeyer, and Dulk, and it is said to have been recently detected in guano, by Unger.

Urinary calculi which contain this ingredient are dissolved in caustic potash; the uric oxide is precipitated from the filtered

<sup>1</sup> See Appendix I, Note 20.

<sup>2</sup> Erdmann has sometimes found hippuric, and at other times benzoic acid, in the urine of the same horse. In all probability an excess of nourishment favours the production of this acid, for the urine of well-fed horses usually contains hippuric acid, while only benzoic acid can be discovered in the urine of horses employed for agricultural purposes: sometimes, however, the latter contains hippuric acid on some days and not on others, without any perceptible cause. For Liebig's theory of the origin of hippuric acid, see 'Animal Chemistry,' pp. 82, 140.

solution by a stream of carbonic acid. It forms a white precipitate, which, when dried, constitutes a pale yellow hard mass. It is represented by the formula<sup>1</sup>  $C_{10} H_4 N_4 O_4$ . It differs from uric acid in containing two atoms less oxygen, hence the name of uric oxide. It dissolves in the alkalis, in small quantity in hot water, hydrochloric and oxalic acids, it is insoluble in alcohol and ether, and produces no effect on test paper. It dissolves also in concentrated sulphuric acid with a yellow colour, and no precipitate is caused by the addition of water to the solution. It is soluble in hot nitric acid *without effervescence*,<sup>2</sup> and more slowly than uric acid. On carefully evaporating this solution, a lemon-yellow residue is left, which is not reddened by the vapour of ammonia, but which is dissolved with a reddish yellow colour by caustic potash, and leaves, on evaporation, a red residue. Muriate of ammonia throws down a yellow precipitate from the potash solution. Uric oxide differs from uric acid in being insoluble in a dilute solution of carbonate of potash; by this property these two substances may be separated from one another when they occur together.

Dulk conceives that he has effected the metamorphosis of uric oxide into uric acid. The yellow nitric-acid solution of uric oxide was evaporated on a watchglass to a thick consistence. After a few days, small, hard, and transparent crystals appeared. A little of the portion which remained fluid, when heated on a platinum spatula over the flame of the spirit-lamp, assumed a blood-red tint, and in a few days the fluid which remained in the watchglass, exposed to the atmosphere, underwent a similar change of colour. He considers the small crystals which were formed to consist of alloxantin; and, in support of his view, he alleges the following facts. Cold water poured over them assumes a red tint, but does not dissolve them; they are, however, perfectly soluble in boiling water, and, on the addition of ammonia to a hot concentrated solution, a reddish colour manifests itself, which disappears on cooling. On concentrating a portion of the solution to a few drops, mixing it with nitric acid, and then adding ammonia, a greenish salt separated itself.

Lehmann instituted a series of experiments with the view of

<sup>1</sup> See Appendix I, Note 21.

<sup>2</sup> Dulk states that, in his case, the uric oxide did slightly effervesce.

obtaining uric oxide from uric acid by the action of deoxidising agents, but he failed in his attempt.

### 16. *Cystin*.

*Cystin, cystic oxide.* Cystin is an occasional constituent of urinary calculi, and is sometimes found as a crystalline deposit in the urine. It may be obtained by dissolving a portion of one of these calculi in caustic potash, and adding acetic acid to the boiling solution. As the fluid slowly cools, the cystin separates in six-sided, colourless, transparent scales. It may also be obtained in crystals from a solution in caustic ammonia, if left to evaporate slowly. The scales are then thicker, and may be considered as regular six-sided prisms.

Cystin has an extraordinary composition. It contains 25·5% of sulphur. Its formula<sup>1</sup> is  $C_6 H_6 N O_4 S_2$ .

It has neither an acid nor alkaline reaction; when heated, it does not melt; takes fire with a blueish flame, and gives off a very characteristic odour; is very slightly soluble in water, and quite insoluble in alcohol; dissolves in dilute sulphuric, nitric, hydrochloric, phosphoric, and oxalic acids, the saturated solutions yielding, on gentle evaporation, salt-like compounds of cystin and the acid; these compounds separate in diverging crystalline needles, which have an acid taste, and are not very durable. Cystin dissolves readily in the fixed alkalies, and forms, on evaporation, granular crystals. It dissolves in caustic ammonia, but does not combine with it. Carbonate of ammonia, is the best reagent for throwing it down from its acid solutions, as it does not dissolve cystin. It may be removed from an alkaline solution by acetic, citric, or tartaric acid, with none of which it enters into combination: acetic acid is generally used.

*Diagnosis of cystin.* Cystin may be recognized by the peculiar crystalline form<sup>2</sup> (six-sided plates) in which it separates from its solutions; by its insolubility in water and alcohol; by its behaviour towards acids; and by its peculiar odour on burning. Its crystalline form and its behaviour towards acids distinguish it clearly from uric acid: these tests, as well as its solubility in hydrochloric and oxalic acids distinguish it from uric oxide.

<sup>1</sup> See Appendix I, Note 22.

<sup>2</sup> I once observed an amorphous deposit of urate of ammonia yield, on the addition of acetic acid, perfectly regular hexagons. This form is also depicted by Rigby, in his work on Dysmenorrhœa.

## CLASS II. NON-NITROGENOUS CONSTITUENTS.

1. *Animal Sugars.*

*a. Sugar of milk* is an integral constituent of the milk of the mammalia, and is a very rare ingredient of any other fluid. It has never been detected with certainty in the blood; although Simon was led to believe, from the taste, and the carbonization with sulphuric acid, that he had once separated it from calves' blood. Prout once found it in the liquor amnii of a cow, but this is the only instance in which it has been detected in that fluid. A more remarkable case is recorded by Koller,<sup>1</sup> who removed a milky-looking fluid from between the tunics of the testicle, which contained sugar of milk.

Sugar of milk may be obtained by evaporating whey to the consistence of a syrup, and setting it aside for some weeks in a cool place. Granular crystals of sugar of milk will be spontaneously deposited. In order to procure them in a state of purity they require several solutions and recrystallizations.

Sugar of milk is white, and crystallizes in right four-sided prisms usually terminated by four-sided pyramids, which are semi-transparent, and have a spec. grav. 1.543. It dissolves in 5 or 6 parts of cold water, and in 2.5 parts of boiling water, without forming a syrup. A solution communicates a more decidedly sweet taste to the tongue than the crystals themselves. Sugar of milk is unaltered by the air, loses nothing at 212°, and is insoluble in alcohol and ether. At a high temperature it fuses, swells up, and develops a sweetish but very pungent odour. It burns with a palish blue flame, and leaves after incineration, an ash consisting of the carbonates, sulphates, and phosphates of lime and potash, amounting to about 1% of the sugar. According to Simon, the sugar of woman's milk does not melt on being exposed to a high temperature, but only becomes tough and fibrous.

By digestion in dilute sulphuric or hydrochloric acid, or in

<sup>1</sup> This fluid contained in 1000 parts: Butter 16.49—casein 20.31—sugar of milk 31.50—chloride of sodium 2.78—lactate of soda 0.74—sulphate of potash 1.51—sulphate of soda 0.37—carbonate of lime 0.38—carbonate of magnesia 0.47—phosphate of magnesia 0.89. (Wagner's Handwörterbuch, t. i, p. 25.)



acetic or citric acid, sugar of milk becomes converted into sugar of grapes. By nitric acid it is decomposed into mucic,<sup>1</sup> oxalic, saccharic, and carbonic acids.

On the addition of casein, animal membrane, diastase, &c. to a solution of sugar of milk, lactic acid is formed and the fluid begins to ferment.

Crystals of sugar of milk may be represented by the formula  $C_{12}H_{12}O_{12}$ . At a temperature of  $212^{\circ}$  the crystals lose  $11.9\%$ , or two equivalents of water. Consequently the formula for anhydrous sugar of milk is  $C_{12}H_{10}O_{10}$ .

$\beta$ . *Diabetic sugar* exists in the blood and urine, and occasionally also in the sweat<sup>2</sup> of persons suffering from diabetes.

It may be obtained by adding basic acetate of lead to the urine, filtering, precipitating any excess of lead by sulphuretted hydrogen, evaporating, extracting the syrupy residue with alcohol, and allowing the alcoholic solution to crystallize. It requires several crystallizations to obtain the sugar in a state of purity. Diabetic sugar usually crystallizes in wart-like knots, or plumose groups, of minute, rhombic, transparent crystals. It is white, devoid of odour; in sweetness and in solubility in water<sup>3</sup> it ranks between cane sugar and sugar of milk. It is more soluble in dilute alcohol than sugar of milk, but is insoluble in absolute alcohol and ether.

Diabetic sugar in a crystalline state is represented by the formula  $C_{12}H_{14}O_{14}$ ; in this condition it contains two equivalents, or  $9\%$  of water, so that its correct formula is  $C_{12}H_{12}O_{12} + 2HO$ . It is identical in its chemical composition with sugar of grapes.

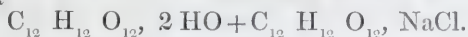
Diabetic sugar forms a beautiful crystallizable compound with chloride of sodium. On saturating diabetic urine with common salt, and leaving it to spontaneous evaporation, crystals three fourths of an inch in diameter may be obtained. They are not very regular in their form, but most of them are six-sided double pyramids. These crystals are hard, easily pulverizable, transparent, of a combined saltish and sac-

<sup>1</sup> It is worthy of remark that sugar from different sorts of milk yields varying quantities of mucic acid.

<sup>2</sup> A case in which sugar was detected in the sweat of a diabetic patient is recorded by Nasse, Rhein. Corresp. Blatt. 1842. Nr. 6.

<sup>3</sup> Simon found that one part of diabetic sugar dissolved in 1.3 of water at  $53^{\circ}$ .

charine taste, and dissolve in about 3·7 parts of cold water, and slightly in alcohol. The formula for this combination is



*Tests for Diabetic Sugar.*<sup>1</sup> *a. Hünefeld's test.* Place 4 oz. of the suspected urine in a glass exposed to the sun's rays, and add about 6 drops of a tolerably strong solution of chromic acid. In a few minutes if sugar be present, the mixture, previously orange red, becomes brownish, and soon after assumes a bistre-brown colour. These changes take place much more quickly if the mixture of urine and chromic acid be gently warmed before exposure to light.

This test depends for its action upon the deoxidizing power of the sugar, by which the chromic acid is reduced to oxide of chromium; for, after warming the mixture, the addition of a few drops of *liquor potassæ* produces a copious deposit of the green oxide.

There is an important objection to this test which renders all its indications liable to serious fallacy, depending upon the fact, that all urine containing a normal proportion of colouring matter deoxidizes chromic acid; and consequently urine, whether saccharine or not, will partially convert this acid into the oxide. This change certainly does not occur so readily in non-saccharine urine as in a diabetic state of that fluid, but still is sufficiently marked to prevent Hünefeld's test being regarded in any other light than a fallacious one.

*b. Runge's test.* Allow a thin layer of the suspected urine to evaporate on a white surface, as the bottom of a white plate, and, whilst warm, drop upon the surface a few drops of sulphuric acid, previously diluted with 6 parts of water. With healthy urine, the part touched with the acid becomes merely of a pale orange colour, from the action of the latter upon the colouring matter of the urine; whilst if sugar be present the spot becomes deep brown, and soon black, from the decomposition of sugar by the acid, and consequent deposition of carbon. This test is stated to be so delicate, that 1 part of sugar dissolved in 1000

<sup>1</sup> The following observations are principally taken from an excellent paper, by Dr. G. Bird, on the detection of a diabetic state of the urine, in the London Medical Gazette for 1843. We have omitted to notice the test afforded by the rotatory power of a solution of sugar on a ray of polarized light, as it has been shown by Dr. Leeson to afford very fallacious results. Memoirs of the Chemical Society, Part 7.

of urine can be readily detected; and even when mixed with 2000 parts the indications are tolerably distinct.

According to Dr. G. Bird, the presence of albumen causes the acid to yield a tint nearly resembling that produced by sugar.

*c. Moore's test* depends on the conversion of diabetic sugar into brown melassic (or perhaps sacchulmic acid) under the influence of a caustic alkali. Place in a test tube about two drachms of the suspected urine, and add nearly half its bulk of *liquor potassæ*. Heat the mixture over the spirit-lamp, and allow it to boil for a minute or two; the previously pale urine will become of an orange-brown or even bistre tint, according to the proportion of sugar present. This reaction has been long known, but Mr. Moore deserves the credit of bringing it prominently forward.

*d. Trommer's test.* Add to the suspected urine contained in a large test tube, a few drops of a solution of sulphate of copper; a very inconsiderable troubling generally results, probably from the deposition of a little phosphate of copper. Sufficient *liquor potassæ* should then be added to render the whole strongly alkaline; a grayish green precipitate of hydrated oxide of copper falls, which, if sugar be present, wholly or partly redissolves in an excess of the solution of potash, forming a blue liquid, not very unlike the blue ammoniuret of copper. On gently heating the mixture nearly to ebullition, the copper falls in the state of suboxide, forming a red and copious precipitate. If sugar is not present, the copper is deposited in the form of black oxide.

This test is founded on a fact long known, but not previously applied to the detection of sugar, of the power possessed by some organic matters of reducing oxide of copper, as well as some other oxides, to a lower state of oxidation. It certainly is the most delicate of all the chemical tests hitherto proposed for the detection of sugar in the urine, and will readily detect it in diabetic urine, even when very largely diluted.

It is important in using this test that no more of the solution of sulphate of copper be used than is sufficient to afford a decided precipitate on the addition of the *liquor potassæ*. If this precaution be not attended to, a part only of the black oxide will be reduced to red suboxide, unless a very large quantity of sugar is present, and thus the indications afforded by this test will be rendered indistinct.

*e. Fermentation test.* The development of the vinous fermentation on the addition of a little ferment or yeast to a fluid, has long been applied as a test for the detection of sugar. It was successfully employed by Professor Leopold Gmelin of Heidelberg<sup>1</sup> for the detection of sugar in the animal fluids after the ingestion of amylaceous food. Dr. Christison has the merit of particularly suggesting the application of fermentation for the discovery of a diabetic state of the urine.

When a little yeast is added to healthy urine exposed to a temperature of about 80°, no other change occurs for some time, except the development of a portion of carbonic acid mechanically entangled in the yeast. When sugar is present in the urine thus treated, it soon becomes troubled, a tolerably free disengagement of bubbles of carbonic acid takes place, and a frothy scum forms on the surface of the fluid, which evolves a vinous odour. These changes take place with great rapidity, even when the quantity of sugar present is very small. If the evolved carbonic acid is collected, the quantity of sugar in the urine may be determined by measuring it, as a cubic inch<sup>2</sup> of the gas very nearly corresponds to a grain of sugar.

In the absence of a mercurial trough, the carbonic acid may be determined by the increase of weight<sup>3</sup> of Liebig's bulb-apparatus, charged with a solution of potash.

*f. Test afforded by the growth of the torula.* If urine containing the smallest proportion of sugar be exposed for a few hours to a temperature above 70°, and a drop taken from the surface be examined under the microscope, numerous very minute ovoid particles will be discovered. In the course of a few hours more they become enlarged, and appear as distinct oval vesicles, which rapidly become developed into that species of confervoid vegetation, to which the term *torula* has been applied.

## 2. Fats.

Under the name of "fats," we include various non-nitrogenous compounds, which are insoluble in water, but soluble in hot alcohol and ether.

<sup>1</sup> Recherches Expérimentales sur la Digestion. Paris, 1826. Part I, p. 202.

<sup>2</sup> 100 cubic inches of carbonic acid gas correspond with 106.6 grains of diabetic sugar.

<sup>3</sup> 100 grains of carbonic acid indicate 225 grains of diabetic sugar. The gas must be passed through a tube containing chloride of calcium.



Some of these fats possess the property of being decomposed by strong bases, especially by the alkalies, and by oxide of lead; in this case one of the two principal constituents separates itself, while the other (an acid) combines with the base, forming a soap with the alkalies and a plaster with oxide of lead. Hence it follows that those fats which, on account of this property, are termed saponifiable, are, like the salts, formed of an acid and of a base; these acids and their bases being themselves the oxides of compound radicals, probably of hydro-carburets.

There are other fats which cannot be decomposed in this manner: they are termed non-saponifiable fats.

We shall commence with the consideration of the former class, the *saponifiable or true fats*.

*a. Fatty Bases.* We are acquainted with three bodies, oxides of different radicals, which act the part of bases in the animal fats. These are *glycerin*, the *oxide of cetyl*, and *cerain*: the first of these three is the most widely distributed, and forms the base of the fats of the human body; the oxide of cetyl exists in spermaceti, and cerain in bees' wax. We shall restrict our remarks to glycerin.

*Glycerin*<sup>1</sup> is separated from the fats by the act of saponification, when the acid with which it was combined enters into combination with the new base. The best method of obtaining it in a state of purity is to boil an animal fat with oxide of lead. The salt of lead which is formed is insoluble in water, (it is, in fact, a plaster,) while the glycerin remains in solution. After removing any excess of lead by a current of sulphuretted hydrogen, we must evaporate the fluid *in vacuo* over sulphuric acid.

The glycerin, prepared in this manner, is a clear uncrystallizable fluid, of spec. grav. 1.28, of a yellowish colour, devoid of odour, of a marked sweet taste, very soluble in water and alcohol, but insoluble in ether. It burns with a clear blue flame. It is considered as the hydrate of an oxide of a radical, *glyceryl* ( $C_6 H_7$ ), which has not yet been isolated. Its composition is expressed by the formula<sup>2</sup>  $C_6 H_7 O_5 + HIO$ . Stenhouse

<sup>1</sup> This substance, glycerin, is united in each fat with a different acid, and hence the fats may be considered as salts of glycerin.

<sup>2</sup> See Appendix I, Note 23.

assigns the formula  $C_3 H_3 O$ , or  $C_3 H_2 + O$ , and Redtenbacher  $C_6 H_4 O_2 + 4 HO$ , to this substance. At an elevated temperature, a portion of the glycerin is distilled without change, while the rest is converted into empyreumatic oils, acetic acid, and combustible gases, leaving a carbonaceous residue.

*Diagnosis.* Glycerin may be recognized by its taste, by its solubility in water and alcohol, but not in ether, by the absence of crystallization, and by the strong white precipitate which is formed upon the addition of nitrate of mercury.

*β. Fatty Acids.* We shall now proceed to consider the fatty acids, which, in combination with glycerin, constitute the various fats and oils. Two simple fats, *stearin* and *margarin*, and a simple oil, *olein*, with their respective acids, the *stearic*, *margaric*, and *oleic*, are especially deserving of notice.

The researches of Redtenbacher, Varrentrap, and Bromeis, have shown that the two former of these acids are in reality constituents of the same radical, in different stages of oxidation. This radical is termed *margaryl*, and its constitution is expressed by the formula  $C_{34} H_{33}$ .

In addition to these acids, we find certain fatty acids in butter, which, in combination with glycerin, form distinct fats. Frémy has likewise described a peculiar acid of this nature as existing in the brain, to which he has given the name *cerebric acid*. We omit the consideration of various other fatty acids, which are only met with in particular animals and in the vegetable kingdom.

*a. Margaryl and its oxides—stearic and margaric acids.* On saponifying mutton-fat with potash, dissolving the soap which is thus formed in six parts of hot water, and then adding forty-five parts of cold water, and allowing the solution to rest at a temperature of  $60^\circ$ , we obtain, after some little time, a lamellar precipitate of bistearate of potash, mixed with bimar-garate, and a little oleate of the same base. On neutralising the free potash in the supernatant fluid with an acid, and proceeding as before, we obtain a precipitate of the margarate and stearate of potash. After this process has been repeated several times, nothing but oleate of potash remains in solution. The precipitates must be washed, dried, and dissolved in boiling alcohol. On cooling, the stearate of potash, which is the least soluble,

separates first, mixed with a small quantity of the margarate. The more frequently the solution is repeated the more certain are we that ultimately the whole of the margarate will be retained in solution.

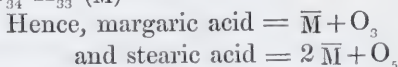
The pure stearate of potash is decomposed by warm dilute hydrochloric acid; and the *stearic acid* which precipitates is to be washed in water and dissolved in boiling alcohol, from which it crystallizes, on cooling, in white brilliant scales. By the same process the *margaric acid* is separated from the pure margarate of potash. Margaric acid is obtained most easily from human fat, which contains a very large amount of margarin. Stearic acid melts at  $158^{\circ}$ . The specific gravity of the acid in its solid state is 1.01. It is perfectly insoluble in water, but dissolves readily in ether as well as in boiling alcohol, in which, on cooling to  $122^{\circ}$ , crystals begin to form. Its solution exhibits a mild acid reaction towards litmus; in the solid form it burns with a clear flame, like wax.

The leading difference between margaric and stearic acids is the greater fusibility of the former, which becomes liquid at  $140^{\circ}$ . Its crystals assume an acicular form, and are smaller and less brilliant than those of stearic acid.

Stearic acid is represented by the formula<sup>1</sup>  $C_{68} H_{66} O_5$ . In its crystalline state it is combined with 2 atoms of water (forming the hydrate of stearic acid), which it gives up on uniting with a base.

Margaric acid is represented by the formula  $C_{34} H_{33} O_3$ . The hydrate contains only 1 atom of water.

The radical of these two acids, *margaryl*, is represented by the formula  $C_{34} H_{33} (\overline{M})$



If we treat stearic acid for some time with nitric acid at a temperature of  $212^{\circ}$ , it becomes completely converted into margaric acid.

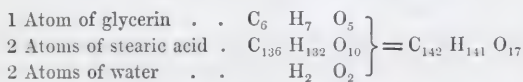
A similar, although not so perfect an effect is produced by sulphuric and chromic acids.

The stearic and margaric are very weak acids; at an elevated temperature they have the power of expelling carbonic acid

<sup>1</sup> See Appendix I, Note 24.

from its combinations; most of the other acids, however, decompose their salts. The alkaline and neutral stearates and margarates are soluble in water; the acid salts (for there are bi- and even quadri-stearates of potash and soda) are not soluble in this fluid, neither are the salts formed with other bases. The stearates of baryta, strontia, and lime are white, insipid, and inodorous powders. The neutral stearates of potash and soda occur in many of the animal fluids, especially in the bile.

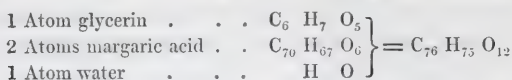
We have already observed that most of the fats are formed by a combination of stearic and margaric acids with glycerin. The *bistearate of glycerin*, or, as it is usually termed, *stearin*, is best obtained from mutton suet, either by washing it with ether as long as anything is dissolved, or by mixing up melted suet with six times its volume of ether, and subjecting the mass, when cold, to strong pressure. In both these processes the olein, which is fluid at the ordinary temperature, is removed, and the stearin remains behind, although seldom in a state of purity. Stearin melts at  $144^{\circ}$ . It is insoluble in water, and only dissolves in alcohol with the aid of heat. It dissolves very readily in boiling ether; but, as the ether cools, nearly the whole of the stearin is again precipitated, and at  $59^{\circ}$  it only retains the one hundred and twenty-fifth part of its weight in solution. It is also soluble in the fatty and volatile oils, and in pyroacetic spirit. The stearin, after being melted down, and allowed to reassume its solid form, appears as a white, semitransparent, uncrystalline mass, not unlike wax. Acids and bases convert it into stearic acid and glycerin. The formula for stearin is  $C_{142} H_{141} O_{17}$ ; it is equivalent to



The *bimargarate of glycerin*, or *margarin*, is obtained by submitting to spontaneous evaporation the ethereal solution from which the stearin has been separated. The flocculi of margarin that separate themselves must be freed from olein by pressure. Margarin melts at  $118^{\circ}$ . Its solubility in ether is much greater than that of stearin; at  $74^{\circ}$  it is perfectly soluble in 5 parts of ether. It is nearly as soluble in alcohol at the ordinary temperature as at the boiling point. In other respects it closely resembles stearin.



The formula for margarin is  $C_{76} H_{75} O_{12}$ , corresponding with



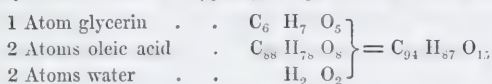
*b. Oleic acid.* This acid is obtained from the oleate of potash, which is produced during the preparation of the stearate and margarate of potash, and remains in solution. It must be separated by the addition of a mineral acid, and then well washed and shaken in hot water. It is an oily fluid, of a clear yellow colour, and does not assume a solid form until it is cooled several degrees below the freezing point of water. At about  $19^\circ$  or  $20^\circ$  it congeals into white acicular crystals. It is very acid, and has a rancid odour and taste. Its specific gravity is 0.898. It is not soluble in water, but dissolves in alcohol in all proportions, and the spirituous solution acts freely on litmus paper. It combines with stearic and margaric acids in all proportions, and the perfect separation of the acids in such cases is not very easy. Its composition, according to Varrentrap, is represented by the formula  $C_{44} H_{39} O_4 + HIO$ .

Oleic acid may be distilled *in vacuo* without undergoing any change; but if atmospheric air be admitted, a small portion only passes over unaltered, while the greater part is decomposed, and some carbon remains in the retort.



Sebacic acid was formerly considered as a product of the destructive distillation of all fatty bodies, but it has been shown by Redtenbacher to arise only from oleic acid. Oleic acid removes carbonic acid from bases. The oleates do not crystallize; those which are soluble appear as soft, easily fusible bodies, and are more soluble in alcohol than in water. The oleates of potash and soda, if treated with a sufficient quantity of water, become reduced to binoleates, and a portion of the base is freed. The oleate, as well as the stearate of soda, exists in the bile. The *binoleate of glycerin*, usually termed *olein*, exists in small quantity in the various solid fats, but forms the principal mass of the liquid fixed oils. It exists as an oleaginous fluid, and varies in some respects, especially in regard

to the point of fusion in the fats of different animals. Chevreul describes the olein of human fat as a colourless oil, devoid of odour, and of a sweetish taste, which retains its fluid state at  $25^{\circ}$ . At a lower temperature it assumes a crystalline acicular form. Its specific gravity at  $59^{\circ}$  is 0.913. One hundred parts of boiling alcohol dissolve 123 of olein; when the solution cools to  $170^{\circ}$ , it becomes turbid. It is readily soluble in ether, but perfectly insoluble in water. It burns with a clear flame. It dissolves camphor, phosphorus, selenium, the ethereal oils, benzoic and many other organic acids. Its composition is represented by the formula  $C_{94} H_{87} O_{15}$ , and is composed of



*c. Butyric and its allied acids.* Butter contains four volatile acids, which stand in a very simple relation to each other, namely, *butyric acid* =  $C_4 H_8 O_2$ , *caproic acid* =  $C_{12} H_{24} O_2$ , *capryllic acid* =  $C_{16} H_{32} O_2$ , and *capric acid* =  $C_{20} H_{40} O_2$ . Butter sometimes affords, instead of butyric and caproic acids, a distinct acid, *vaccinic acid*, which appears to be equal to the sum of those two acids, minus 1 atom of oxygen, and is very readily decomposed into them. Two of these acids, the capryllic and vaccinic, were discovered only a few months ago, by Lerch, a German chemist. The following is the method that he gives for their separation:

"Fresh butter is completely saponified with potash in a still, the soap decomposed in the vessel with dilute sulphuric acid, the head then luted on, and the aqueous liquid drawn off to within a fourth. Fresh water is then added to it, which is again distilled off, and this operation continued as long as the water which passes over possesses any acid reaction. In this manner the volatile fat acids are carried over just as the essential oils; the action of the atmosphere is moreover entirely excluded. From four to five pints of a milky liquid are obtained from a pound of butter, on the surface of which float drops of oil and particles of hard or smeary fat. The distilled water is immediately saturated in the receiver with barytic water, and allowed to stand well closed till the end of the distillation. When the distillation is finished, the still is cleansed, and the liquid saturated with barytic water, evaporated in it, with the head on,

to about the twentieth part, and the still hot concentrated ley then reduced to dryness in a retort.

“The saline mass obtained in this manner consists of two portions, one easy, the other difficult of solution. The more soluble portion consists, according to circumstances, of butyrate and caproate of baryta, or solely of the barytic salt of vaccinic acid; but in this case there is little or no butyric or caproic acid present. The portion difficult of solution consists of the baryta salts of two distinct acids, which Chevreul described together as caprate of baryta. The more insoluble portion amounts to about the twentieth part of the soluble, and the entire mass to about the tenth part of the saponified butter. To separate the different salts, the residuary saline mass is boiled with about 5 or 6 parts of water; one portion dissolves, the other remains behind. The solution of the readily soluble salts is set aside to crystallize; if, on the first crystallization, the crystals which separate have the appearance of benzoate of lime, and do not effloresce, *i. e.* if they are caproate of baryta, the butyrate of baryta has still to be sought for in the solution; but if nests of small crystals form, which quickly effloresce, and resemble nests of the native carbonate of lime, it is vaccinate of baryta, and it is then unnecessary to look for butyrate and caproate of baryta.

“The circumstances under which butter contains vaccinic acid or butyric and caproic acids are not known. The butter of 1842, and likewise that of the following winter, contained, in several experiments, not a trace of any other easily soluble salt of baryta than the vaccinate; while the butter in the summer of 1843 contained no vaccinic acid, but only the other two.

“The soluble saline mass, containing the butyric and caproic acids is dissolved in water and evaporated to crystallization, in order to separate them. Long silky needles, aggregated in bundles, separate even in the first crystallizations; and if the solution has been sufficiently concentrated, nearly the whole of the caproate salt is deposited. The entire solution solidifies to a paste of minute needles, which are separated by pressure from the mother-ley, and purified by recrystallization. The remaining ley is now allowed to crystallize spontaneously, which is best effected by exposure to the sun; at first a little caproate of baryta still separates, the form of the crystal then changes, laminae of mother-of-pearl lustre make their appearance, and all the

subsequent crystallizations are nearly pure butyrate of baryta, which is purified by recrystallization.

"The saline mass of difficult solution is dissolved in just so much boiling water as is requisite for complete solution, and is filtered while hot. During the cooling, the liquid becomes filled with minute scales of caprate of baryta, of a fatty lustre, which subside in the form of a crystalline precipitate. The decanted mother-ley is again evaporated one fourth, when a fresh quantity of caprate of baryta separates. This salt is purified by recrystallization. The mother-ley now contains the capryllate in solution; it is evaporated by exposure to the sun, when the salt separates in minute granules and verrucous masses, which are obtained pure by recrystallization.

"This is the best method of separating these salts from each other; an absolute separation is impossible, for there always remain mixed crystals and leys, which in small quantities are not worth while working."<sup>1</sup>

The butyrate of baryta is much the most soluble of these salts, requiring only 2.77 parts of water. On decomposing it by adding dilute sulphuric acid to its solution we obtain butyric acid, in the form of a colourless or faintly yellow oleaginous fluid.

Butyric acid possesses an unpleasant odour, which calls to mind at the same time that of acetic acid and of rancid butter. It is soluble in every proportion in water and alcohol, and more soluble in ether than the other acids of the same group. Its specific gravity is 0.963 at 59°; it evaporates easily in the open air, boils under ordinary pressure at about 327°, and distils without undergoing any perceptible alteration. Its vapour is inflammable, and burns with a blue flame. A continued cold of 4° does not produce any change in the state of the butyric acid; its taste is strongly acid and burning; it attacks and disorganizes the skin in the same manner as the strongest acids.

The chemical relations of this acid have been made an object of especial research by Chevreul, Pelouze and Gélis, and Lerch; and numerous butyrates and butyric ether have been formed, and submitted to careful investigation and analysis.

<sup>1</sup> Ann. der Chem. und Pharm. xlix, p. 212, as translated in Number 45 of the Chemical Gazette.



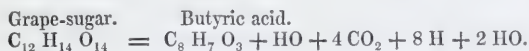
The only compound of butyric acid that concerns us at present is the *butyrate of glycerin*, or *butyrin*, the essential fatty matter of butter. In order to isolate butyrin from the various compounds with which it is associated in butter, we must adopt the following method. Purified butter must be kept for some days at a temperature of about 66°. At that temperature olein and butyrin are liquid, while the solid stearin forms a mass by degrees, so that the liquid portion may be decanted off. On this decanted oily matter its own bulk of absolute alcohol must be poured, the mixture must be left for twenty-four hours, and the temperature be regulated to 66°. On distilling off the alcohol from this alcoholic solution a residue of butyrin is left, mixed with a little olein. A slightly acid reaction is usually observed, in consequence of the decomposition of a little of the butyrin into butyric acid. This may be removed by digesting the butyrin in a mixture of magnesia and water. A butyrate of magnesia, soluble in water, is formed, and the butyrin may then be obtained perfectly neutral. The removal of all traces of olein from butyrin is nearly impossible.

Butyrin occurs as a colourless oil, which solidifies at 32°, is soluble in cold alcohol, but not in water, is devoid of odour, and produces no effect on litmus. In a warm atmosphere it speedily decomposes, and yields butyric acid. M. M. Pelouze and Gelis have recently shown that by a peculiar process of fermentation butyric acid may be obtained from sugar. They recommend the following as the best process for obtaining the largest possible amount of butyric acid from this source.

“ A small quantity of casein is mixed with a solution of sugar, indicating 10° on the saccharometer, and sufficient chalk to saturate the whole of the butyric acid which subsequently forms. This mixture is left at a constant temperature of from 77° to 86°. It soon undergoes very considerable alterations; the fermentation, at first viscous, subsequently lactic, gradually becomes butyric. These decompositions are sometimes successive, sometimes simultaneous, without its being possible to regulate their course. The disengagement of gases becomes more abundant, and analyses show that a period arrives when the free hydrogen amounts to a third of the volume of the carbonic acid. At this period the butyric fermentation is in all its vigour; when at last, at the end of some weeks, all disengage-

ment of hydrogen has ceased, the operation is at an end, and the solution then contains only butyrate of lime."

The composition of butyric acid, its proportion which amounted in several experiments to above the third of the weight of the sugar, the liberation of free hydrogen, and of carbonic acid (independent of that which is disengaged from the chalk,) admit of our supposing that, under the prolonged influence of ferments, sugar is decomposed in the following manner :



This formula is merely intended to exhibit the final result, for several chemical processes<sup>1</sup> precede the formation of butyric acid.

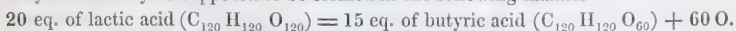
By combining the butyric acid formed in this manner with glycerin, they obtained a fatty matter that seemed in all respects identical with butyrin, as described by Chevreul.

Fibrin yields butyric acid as one of the products of its decomposition: the other products of its putrefaction are albumen, carbonic and acetic acids, and ammonia. It may likewise be obtained by heating this substance with potash at a temperature of from 320° to 356°. A small quantity of a volatile fatty acid forms, which remains in combination with the potash, whilst ammonia and other volatile products are disengaged. This acid has not yet been analysed, but it seems to possess all the properties of butyric acid. (Wurtz.)

*Caproic acid* is obtained from the caproate of baryta, which crystallizes in long silky needles, aggregated into bundles.

It is an oily limpid liquid with the odour of sweat, and a sharp acid taste. Its spec. grav. is 0.922 at 72°; it evaporates in the open air; its boiling point is above 212°, and it is soluble in 96 parts of water at 44°.6. It dissolves in alcohol and ether.

<sup>1</sup> It is well known that if a small quantity of casein be introduced into a solution of cane-sugar or sugar of milk, lactic acid begins very soon to be formed. The butyric acid may be supposed to be formed in the following manner:



These 60 eq. of oxygen decompose 6 eq. of lactic acid, and we have—



when the carbonic acid is exactly three times the volume of the hydrogen produced.

*Capryllic acid*, at the ordinary temperature, forms a smeary mass; below  $50^{\circ}$  it crystallizes in needles, which are of difficult solution in water, have an acid and acrid taste, and a peculiar disagreeable odour. The baryta salt separates from hot solutions in brilliant laminæ, but on spontaneous evaporation in white granules. It is anhydrous, is not affected by exposure to the air, does not fuse at  $212^{\circ}$ , and is very sparingly soluble in water.

*Capric acid* resembles capryllic acid in its properties. The baryta salt crystallizes from hot solutions in minute fatty needles and scales, and on spontaneous evaporation likewise in scales, arranged in dendritic groups; it is very difficult of solution, is anhydrous, and is not affected by exposure to the air.

*Vaccinic acid*. Vaccinate of baryta separates in nests of crystals, which have already been described; they contain water of crystallization, effloresce very readily in the air, become very similar in appearance to chalk, and diffuse a strong odour of butter, while pure caproate and butyrate of baryta do not effloresce in the least, and have scarcely any odour. Vaccinate of baryta is soluble in water to about the same extent as butyrate of baryta; the saturated solution is thick like oil. When vaccinate of baryta is dissolved in water, and again evaporated in a retort, it crystallizes from the solution unaltered; but if the crystals are exposed for some time to the air, they at last lose nearly all their odour, and no longer when dissolved crystallize on evaporation, but in their stead crops of caproate and butyrate of baryta are obtained. The same happens when a solution is exposed to the air for any length of time, or boiled in an open dish. No baryta separates in this change, no acid vapours are given off, and the solution remains perfectly neutral. Vaccinic acid therefore saturates exactly the same amount of baryta as the two acids which have originated from it; the relative quantity of the caproate and butyrate of baryta formed is proportionate to the atomic weights of these two salts. If vaccinate of baryta is decomposed by sulphuric acid, with free access of air, and the separated acid removed by distillation, saturated with baryta, and set aside to crystallize, a mixture of caproate and butyrate of baryta only is obtained. On adding some solution

of silver to a solution of vaccinate of baryta, a white caseous precipitate is formed, which is soon reduced, and smells strongly of butyric acid.

Vaccinic acid has, therefore, evidently the same capacity of saturation as caproic and butyric acids together, but probably contains less oxygen.

In all probability these acids form compounds with glycerin, and exist in butter as distinct fats.

The brain contains several distinct fats which have been examined by different chemists (Kühn, Couerbe, Frémy,) and found to contain phosphorus and sulphur. Couerbe has given to these the names of *eleencephol*, *cerebrot*, *cephalot*, and *stearaconot*. Cephalot is the only one that is saponifiable, and which, therefore, comes under the category of the true fats. Its fatty acid is unknown; in fact the whole subject of the brain-fats requires an entire revision.

Frémy<sup>1</sup> has described two fatty acids that exist in the brain in combination with soda, to which he has applied the names of *cerebric* and *oleophosphoric acids*.

Of the bodies just described, those which act the part of bases, never occur naturally in an isolated state; and those which act as acids, very seldom. Butyric acid occasionally exists in a free state in the urine, and, according to Gmelin, in the gastric juice, and occasionally in the cutaneous transpiration. Lecanu states that the margaric and oleic acids exist in a free state in the blood. Some of the fatty acids, as already observed, exist in the bile and in the cerebral matter, in combination with soda, but they are most commonly found united with glycerin.

The contents of the cells of ordinary adipose tissue are a mixture of stearin, margarin, and olein; and the marrow of the bones has a very similar composition. The relative proportions of these three substances varies in the fat of different animals, which is the reason of the different consistence of various fats. The more olein present, the softer and more liquid will the fat be: and those fats in which the olein forms the principal ingredient are called oils. Those of a mean consistence are most properly termed *fats*, while the harder ones

<sup>1</sup> Annales de Chimie, 1841.



are known as *suet*. Stearin is the principal constituent of suet ; margarin of fat or lard. Human fat affords a good illustration of the proper fats. It solidifies at  $62^{\circ}$  ; but the consistence is not constant even in the same person—for instance, the fat of the kidneys is perfectly solid at  $62^{\circ}$ , while the fat of the subcutaneous tissue remains fluid as low as  $59^{\circ}$ .

*The non-saponifiable fats.*

*a. Cholesterin* is a normal constituent of the bile, of the brain, and of the spinal cord. It has been found by Lecanu, Denis, Boudet, Marchand, and Simon, in the blood ; by Fromherz and Guggert in the *vernix caseosa* ; by Breschet, Wöhler, and Marchand in hydrocele ; by Stromeyer in an encysted tumour in the abdomen of a woman ; by Breschet and Barruel in the ovary and testicle in a diseased state ; by Caventou in an abscess of the tooth ; by Lassaigne in a scirrhous structure in the mesocolon ; by Guggert in fungus medullaris ; by Marchand in medullary sarcoma ; and by Drunty in a vesical calculus extracted from a dog. It sometimes exists in a state of solution, while in other cases it floats on the surface, either in the form of brilliant scales, or of solid masses. It has never been found in any of the plants which are used for food ; but Dumas has found a substance of a similar composition in the resin of the pine.

In order to obtain it from biliary calculi, we must first treat these with boiling water, then triturate, dry and pulverize the residue, treat it with boiling alcohol, filter it while still hot, and allow it to cool very gradually. The cholesterin separates itself in the form of white, sparkling, transparent scales. These should be collected in a filter, again dissolved in hot alcohol, and allowed to recrystallize. In this state it will be tolerably pure. Berzelius recommends the previous addition of a few drops of caustic potash or ammonia, in order to saponify any stearic or margarinic acid that may be present.

In order to obtain it from the brain, that organ must first be deprived of all its water, by being finely triturated and then placed upon the water-bath. This being fully accomplished it must be treated with ether, and afterwards with boiling alcohol, until these fluids cease to abstract anything more. As the alcoholic solution cools, a white powder is precipitated. By

gently distilling the ethereal solution, a residue remains, from which cholesterin may be taken up by boiling alcohol; on mixing the two alcoholic solutions, evaporating to one fourth, and allowing the mixture to cool, a portion of the fat separates in the form of a white powder, which consists not merely of cholesterin, but also of a substance which is insoluble in cold ether, the *cerebrot* of Couerbe. If, therefore, we treat this fat with ether, the cholesterin dissolves, while the *cerebrot* remains unacted on. By evaporation we obtain the cholesterin in a crystalline state, and by dissolving it in boiling alcohol and allowing it to recrystallize on cooling, we obtain it in a state of purity.

On slowly cooling its alcoholic solution, cholesterin crystallizes in delicate white nacreous scales. It is devoid of taste and smell, is insoluble in water, but dissolves in alcohol and in ether. According to Chevreul, 100 parts of boiling alcohol of 0.816 dissolve 18 of cholesterin; if alcohol of 0.840 be used only 11.24 parts are taken up: on cooling, the greater part is deposited. Kühn states that 1 part of cholesterin is soluble in 12.1 of ether at 32°, in 3.7 parts at 59°, and in 2.2 parts of boiling ether. Cholesterin is perfectly neutral, of about the same specific gravity as water, and at 280° melts into a colourless fluid without undergoing any decomposition. Crystallized cholesterin contains about 5.2% of water. It burns with a clear flame, like wax, and one of its most striking characteristics is, that it is not affected by a solution of caustic potash.

Its composition is represented by the formula  $C_{37}H_{72}O$ .

*b. Serolin.* This name was given by Boudet to a fatty matter which he discovered in the blood. It has been more recently found and described by Lecanu and Sanson. In order to exhibit it, blood must be first evaporated to dryness on the water-bath, and the residue treated with water as long as anything continues to be taken up. It must then be dried, pulverized, treated with boiling alcohol, and filtered while hot. On cooling, the alcohol deposits this fat in flocculi. It must be collected on a filter, and washed with cold alcohol. Boudet assigns the following characteristics to serolin. It forms flocks of a fatty nacreous appearance, is perfectly neutral, and melts at 97°. On exposing it to a higher temperature, a portion is distilled unchanged, while another part is decomposed into

ammoniacal vapour. In water it is perfectly insoluble, in hot alcohol of .833 it is only slightly soluble, and separates on cooling into its original flocculent appearance, since cold alcohol exerts no solvent influence over it. It dissolves readily in ether. It does not form a soap with caustic potash. Lecanu describes the serolin obtained from human serum, as a white, but not nacreous, substance, which melts at  $95^{\circ}$ , is soluble in ether, but not in watery alcohol.

It may be distinguished from other fats by its insolubility in cold alcohol; from cholesterin, by its lower point of fusion.

*Diagnosis.* The different fats and fatty acids are distinguished by their fusing points, and by their varying degrees of solubility in alcohol and ether.

#### *Lactic, Oxalic, and Acetic Acids.*

1. *Lactic acid* is regarded by most chemists as a constituent of almost all the fluids of the animal body.

The following is the method recommended by Mitscherlich,<sup>1</sup> for the exhibition of pure lactic acid. Sour whey must be evaporated to about one sixth of its volume, and filtered; the phosphoric acid precipitated by lime, and any excess of lime separated by oxalic acid.

After filtration, the liquid must be evaporated to the consistence of a thick syrup, and the lactic acid extracted with alcohol. The alcohol must be removed by evaporation, and the residue dissolved in water mixed with carbonate of lead. In this manner a solution of lactate of lead is obtained, which, after filtration, must be decomposed by sulphate of zinc. Sulphate of lead is immediately precipitated, and lactate of zinc remains in the solution, which must be filtered and evaporated to incipient crystallization. In this manner we obtain crystals of lactate of zinc, a salt only slightly soluble in cold water. Lactic acid may be obtained by converting the lactate of zinc into a lactate of lime or baryta, carefully removing the base by the addition of sulphuric acid, and cautious evaporation.

Pure lactic acid is a colourless liquid, soluble in every proportion in water and alcohol, of a purely acid taste, and so strong and biting as to be almost insupportable. Its formula<sup>2</sup> is



<sup>1</sup> Lehrbuch der Chemie, 1837, p. 512.

<sup>2</sup> See Appendix I, Note 25.

At a red heat lactates with fixed bases are converted into carbonates: 100 parts of the carbonates of potash and soda correspond to 180.9 and 201.1 parts of the respective lactates of those bases.

There is no ready test by which we can detect the presence of lactic acid: it is chiefly distinguished by its negative properties. Rules for the quantitative determination of this acid and its salts will be found in the chapters on the different fluids in which it occurs; they are founded with various slight modifications on the method that we have given for the exhibition of the acid.

2. *Oxalic acid* is not one of the normal constituents of the animal organism; it is however, when combined with lime, a very common ingredient of morbid urine, and of urinary calculi.

*Oxalate of lime*, when obtained by the addition of a soluble oxalate to a salt of lime, occurs as a white amorphous powder, insoluble in water, alcohol, oxalic and acetic acids, but soluble in hydrochloric and nitric acids without effervescence. It leaves, when heated to incipient redness, a white residue of carbonate of lime, from which the amount of oxalate may be easily calculated, for 100 parts of carbonate of lime correspond with 128.9 of oxalate of lime. After a prolonged exposure to a higher temperature, the carbonic acid is expelled, and caustic lime remains.

The occurrence of oxalate of lime in a crystalline state in urinary sediments has been shown, by Dr. G. Bird, to be much more frequent than was formerly supposed; in fact, although the beautiful octohedral forms in which it occurs had been noticed some years ago by Vigla, Donné, and other French observers, it was not until the appearance of Dr. G. Bird's papers in the 'London Medical Gazette' for 1842, that their chemical nature was fully established.

3. *Acetic acid* has been found by Tiedemann and Gmelin in the gastric juice, by Thenard in the sweat, by Simon in the fluid of pemphigus and in saliva, and is asserted by some chemists to be a constituent of urine. For its chemical characters we must refer to any of our systematic treatises on Chemistry: it is sufficient to notice the means by which it may be recognized, and its amount determined. Acetic acid may



be detected by its peculiar odour, which is rendered more obvious by the application of a gentle warmth. The presence of an acetate may be determined by the addition of a little sulphuric acid; the odour of the liberated acetic acid is at once rendered perceptible. The addition of perchloride of iron to free acetic acid produces hardly any visible change, but if it be added to a solution of an acetate, a deep blood-red colour is produced. When acetates and free acetic acid are mixed up with a large quantity of other animal matters, the best method of proceeding is to separate the free acetic acid by distillation. The residue must be evaporated, extracted several times with alcohol, and the alcoholic residue mixed with a little sulphuric acid, and distilled. The first distillation gives the free acetic acid, the second the acetic acid in a state of combination. The amount of acetic acid may be determined by saturating the distilled fluids with potash, evaporating to dryness, and taking up the acetate of potash with alcohol of .833. The acetate of potash obtained by the evaporation of the alcoholic solution is frequently mixed with a little chloride of sodium, the amount of which (if appreciable) may be determined by nitrate of silver.

At a red heat the combinations of acetic acid with non-volatile bases are converted into carbonates.

# CHEMISTRY OF MAN.

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## CHAPTER I.

### ON THE PROXIMATE ANALYSIS OF COMPOUND ANIMAL SUBSTANCES.

Zoochemical analyses are instituted for the purpose of ascertaining, either quantitatively or qualitatively, the proximate or ultimate constituents of animal substances. It is requisite in physiological and pathological chemistry that equal attention should be paid to both these modes of investigation, for there is this great distinction between the chemistry of inorganic and of organic bodies, that in the former case the determination of the proximate principles can be inferred from that of the ultimate constituents, while in the latter case no such rule holds good, and the two species of analyses (the proximate and ultimate) must be conducted separately and distinctly. In the investigation of the variations in the constitution of the blood, whether dependent during health upon age, sex, or temperament, or during disease upon various pathological states of the system ; in the determination of the constituents of milk, sweat, or pus ; in the detection of sugar, urea, or bilin, in the various fluids, in which *normally* they are absent ; in these and all similar cases ultimate analysis will avail us nothing, and we must have recourse to tests for the substances themselves, or for some of their proximate principles. Investigations of this nature will, moreover, do very little for the advancement of pathological or physiological knowledge, unless they are viewed in relation to a considerable number of similar analyses, conducted under precisely corresponding circumstances ; for in consequence of the necessary variation that is constantly occurring in the animal fluids, each analysis can only be regarded as the representative of

one of innumerable varieties, all of which (within certain limits) are equally likely to occur. It is by such a course alone that we can hope to be able to deduce important and trustworthy conclusions regarding the state of the animal fluids in health, and their various deviations from the normal standard, in different states of disease.

A large number of perfectly distinct substances enter into the composition of the blood and urine; neither of these fluids can, however, be regarded as true chemical combinations, but as mixtures of many such combinations, which in their turn are further subject to much variation. The study of these variations in the blood and urine constitutes one of the most important branches of animal chemistry; but in consequence of the immense labour attendant upon a complete analysis of these fluids, it becomes expedient to confine our attention to their most important constituents, in the same manner as the mineralogist seeks only to determine the proportion of ore in a given quantity of a mineral, or the vegetable analyst to ascertain the proportions of sugar, gum, starch, and albumen, while he neglects the non-nutritive substances, the fibre, acids, resins, colouring matters, &c.

All compound animal substances that can fall within the range of our investigation must be embraced in one of the following classes, the solid, the fluid, or the gaseous.

The animal fluids (to which we shall first devote our attention) differ extremely in their composition, but a general scheme may be laid down for their investigation, if we previously know that certain substances are not present, and therefore need not be sought for. Thus, neither urea, uric acid, pepsin, nor bilin will usually be sought for in the milk or in the brain, because it is well known that their formation is limited to certain organs; neither will hæmatin, globulin, nor butyrin be looked for in the bile, nor fibrin in the sweat or in the saliva, nor gluten nor chondrin in any of the normal fluids.

The principle upon which these investigations are conducted is dependent on certain questions, which are to be answered by the analysis. Thus in the analysis of the blood, the principal component parts, the water, albumen, hæmatin, globulin and fibrin, are usually determined; but if it be requisite that the analysis should be more fully carried out, we must separate the hæmatin from the globulin, isolate the fats, extractive matters,

and salts, and determine their individual proportions. This is the plan that I have usually adopted, and in some cases I have added the determination of sugar, urea, and hæmaphæin. The execution of such a comparatively simple scheme as this is a matter requiring considerable time and labour; and if it were required that we should carry out the analysis still further, and separate the various fats, the different combinations of the fatty acids, the varieties of extractive matter, and finally the different salts, our task, in the present state of our knowledge, would be one of great difficulty; and in consequence of the minute proportions in which some of these substances exist in the blood, it would be necessary for us to operate upon a much larger quantity of the fluid than we are usually able to obtain. This method of investigation will probably in a short time be deemed insufficient, for as soon as we have an accurate knowledge of the mode of formation of the extractive matter, its separation and determination will be of the highest importance in explaining many of the phenomena of the metamorphoses of the blood.

The same is the case with respect to the urine. The formation of a perfect quantitative analysis of this complicated fluid is an extremely difficult (if not an impossible) task, in consequence of the facility with which new products are developed during the progress of the investigation. The course usually pursued has been, therefore, the separation of those constituents which are apparently most important, the urea, uric acid, salts, and extractive matter; in some cases the estimation of sugar and albumen has been added. The instances in which the separation of the extractive matter into its three principal groups, and the individual analysis of the salts, have been undertaken, are still more rare.

It has been already observed that a single isolated analysis is of very little intrinsic value, in substances of so varying a nature as the blood or urine. The only method by which we can hope to throw any light upon the leading alterations that occur in these fluids is by the comparison of the results obtained from a series of analyses; and if we were desirous of merely ascertaining so simple a fact as the determination of the pathological states in which either an excess or a deficiency of fibrin and blood-corpuscles occurs in the blood, and the relation that exists between such pathological states and such modifica-



tions of the vital fluid, science would be more benefited by the investigation, than by the performance of a few very perfect analyses, which did not tend to elucidate any particular point.

The best methods for the analysis of the various animal substances which are treated of in this volume, will be found in their proper places. We will, however, give a preliminary sketch of the course that should be adopted, if a fluid, of whose nature we are ignorant, be placed in our hands for analysis.

Such a fluid may contain,

I. The *protein-combinations*: fibrin, albumen, casein, globulin.<sup>1</sup>

II. *Pyin*.

III. *Extractive matters*: water-extract, spirit-extract, alcohol-extract, and their proximate constituents.

IV. *Sugars*: Diabetic sugar, and sugar of milk.

V. *Bilin*, with the products of its metamorphosis.

VI. *Urea*.

VII. The *fats*: olein, stearin, margarin, butyrin, cholesterin, and serolin.

VIII. *Colouring matters*: the pigments of the blood and bile.

IX. The *acids* of the animal body:

a. Fatty acids.

β. Other organic acids.

γ. Inorganic acids.

X. The *bases* of the animal body.

### *General physical analysis.*

1. If the fluid contain flocculi or coagulated matters, they are generally composed of fibrin, which by its spontaneous coagulation frequently includes other substances in a state of mechanical suspension. The whole fluid will sometimes assume a gelatinous consistence, as has been observed in certain products of exudation; in other cases it presents an appearance of separation, one portion assuming the form of a cake or clot, whilst the remainder continues fluid, as in the well-known instance of the blood. On placing these clots, &c., in distilled

<sup>1</sup> Crystallin, or the modification of casein that occurs in the crystalline lens, is not included in this scheme, since it is not known to occur in any of the animal fluids.

<sup>2</sup> [Pyin being tritoxide of protein, must now be regarded as a true protein-compound. The binoxide of protein must also be included in the same category.]

water, the substances which are inclosed by the fibrin gradually separate themselves from it, as for instance albumen, blood-corpuscles, &c., and the fibrin remains devoid of colour, very small in proportion to the clot from which it has been obtained, and forming a membranous, stringy, or flocculent mass.

If the fluid has an acid reaction, the flocculi may arise from coagulated casein, or caseous substances. In this case distilled water has no effect on them. The existence of casein in milk is universally known. Other fluids which contain caseous principles, as for instance, mucus and saliva, usually maintain an alkaline reaction for a considerable period, and thus hold the casein in solution. Pus has usually a neutral reaction, occasionally however pus from the lungs is acid.

If the flocculi are observed to be floating on the surface of the fluid, if they exhibit a frothy appearance, or seem more or less globular, are of a whitish or yellow colour, and possessed of little tenacity, they are composed of mucus, and the microscope will reveal the presence of mucus-granules. A tenacious substance of a yellow or brownish colour, and not unfrequently containing blood, is occasionally found to be deposited in certain animal fluids, for instance, in the urine during *phthisis vesicæ*. It is possessed of more elasticity than mucus, and is very probably composed partially of fibrin, although it is usually regarded as pus.

2. If with the aid of the microscope we can detect blood-corpuscles in the fluid, we may infer the presence of globulin and hæmatin. We recognize the blood-corpuscles, and distinguish them from other objects by their discoid form, and their yellow colour. When blood is mixed with a serous or watery fluid, it frequently happens that the discoid form is no longer apparent; if however a solution of common salt, or of muriate of ammonia be added to a portion of the fluid, the characteristic shape of the blood-corpuscles will be again rendered perceptible. Fluids in which blood-corpuscles are found, are always of a reddish tinge, and invariably contain albumen.

3. The microscope further enables us to detect the following solid forms in fluids: *a*, fat-vesicles; *b*, chyle-corpuscles; *c*, mucus-corpuscles; *d*, pus-corpuscles; *e*, epithelium-cells; *f*, saliva-corpuscles; *g*, various crystalline forms of salts, uric acid, cholesterin, &c.

If the fluid be very viscid and tenacious, mucus-corpuscles are sure to be detected by the microscope: should it yield an ammoniacal odour as if decomposition were going on, the viscosity may be due to the action of the ammonia that has been formed.

4. If the fluid have an acid reaction, a free acid must be present. In most cases this is lactic,<sup>1</sup> occasionally however acetic acid. The latter acid may be recognized by the peculiar odour evolved on the application of heat. It may also be recognized (if the fluid be not very deeply coloured) by the blood-red tint that is produced by the addition of the perchloride of iron, after the free acid has been thoroughly neutralized by ammonia. If acetic be the only free acid, by the time the fluid has been evaporated nearly to dryness, all acid reaction will have disappeared; if however free lactic acid be present, the residue which is left after evaporation will still have an acid reaction.

If the fluid have an alkaline reaction, either a free alkali or an alkaline carbonate must be present. Free ammonia may be recognized by its peculiar odour, and by the vapour which is developed on the approximation of a glass rod moistened with hydrochloric acid.

5. If the fluid have a sweetish taste, it contains sugar. The sweetness is however sometimes not preceptible until the fluid has been evaporated to the consistence of a syrup, or even till the syrup has been treated with alcohol of .900, and the alcoholic solution evaporated. When the presence of sugar is suspected, the various tests mentioned in page 67, more especially Trommer's test, should be applied. If the fluid has a bitter taste, more or less resembling that of bile, it contains either *bilin* or the products of its metamorphosis. The indications afforded by a well-marked saline or acid taste are sufficiently obvious.

6. If the fluid be of a blood-red colour, we may conclude that hæmatin is present; and if blood-corpuscles are detected by the microscope, we have certain proof of the existence of hæmatin, globulin, and albumen. Globulin and hæmatin may

<sup>1</sup> [The presence of this acid in the animal fluids has been recently disputed by Liebig and Enderling; there are, however, too many chemists who assert that they have detected it, to allow us to regard the question as settled in the negative.]

however be occasionally present, when, even after the addition of a solution of salt, sugar, or iodine no blood-corpuscles can be detected; in this case the latter are in a state of perfect solution.

When the fluid is of a dark brown, or blackish-red colour, hæmatin is the colouring constituent. If the fluid be of a clear brown or yellow colour, hæmaphæin is almost sure to be the origin of the tint, especially if any taste of bile be perceptible. Biliphæin will also communicate a yellow, brown, or greenish-brown colour; in this case there is frequently a bitter taste, and on the addition of nitric acid, there is always a change of colour into green or blue, and yellow.

### *Qualitative analysis.*

Having poured the fluid into proper test-glasses, we carry on our investigations in the following manner:

1. If, on the addition of very dilute hydrochloric acid, a precipitate be thrown down, we see whether it will dissolve in an excess of the test.<sup>1</sup> Assuming that the solution is effected, ferrocyanide of potassium is added; if this test instantly throws down a white or yellow precipitate, one or more of the protein-compounds (enumerated in 1) are present.

In order to ascertain which of the protein-compounds has yielded these indications,<sup>2</sup> a portion of the fluid is boiled: if it become turbid, and if the turbidity commence and be most distinct at the surface, or if the fluid coagulate, then albumen is present; in this case nitric acid and bichloride of mercury will throw down copious precipitates. If the fluid become turbid on the application of heat, and the coagulum assume a red tint, then globulin and hæmatin are also present, although the microscope may have failed in detecting blood-corpuscles: in this case, however, the fluid is always of a rather pink or reddish tint.

If the fluid does not coagulate on the application of heat, casein, or one of the caseous substances must be present.

<sup>1</sup> If very dilute hydrochloric acid be employed, the albumen will not be precipitated. (See p. 18.) I prefer hydrochloric to acetic acid, because the latter throws down pyin with the protein-compounds.

<sup>2</sup> Fibrin is recognized by its spontaneous separation, and need not be sought for in the manner indicated in the text.



In this case heat will develop a pellicle on the surface, and acetic acid will throw down a precipitate, which is soluble in an excess of the test: the acid must therefore be added with caution.

It must not however be forgotten that if much albuminate of soda, and at the same time no free albumen be present in the fluid, no coagulation will occur on the application of heat, but a pellicle will be formed on the surface. This is however a case of very rare occurrence, and the difficulty may be readily solved by the addition of acetic acid which will precipitate casein but not albumen. If a fluid which contains casein presents a whitish turbid appearance (as for instance, milk, the milky fluid which is found in the breasts during the later stages of pregnancy, the urine in certain pathological states, &c.) the presence of butter, and in most instances, of sugar, may be inferred.

If the ferrocyanide of potassium does not produce any turbidity in the fluid which has been previously acidulated with dilute hydrochloric acid, *no protein-compound is present.*

2. If the addition of acetic acid to the fluid renders it turbid, or throws down a precipitate, which does not redissolve in an excess of the test, then pyin or mucin<sup>1</sup> is present. In this case, a copious precipitate, insoluble in an excess of the test, is thrown down by alum. In order to show that the precipitate contains no casein, we may dissolve it in dilute hydrochloric acid, and add ferrocyanide of potassium: no precipitate will be thrown down.<sup>2</sup>

3. If allantoin, uric acid, or hippuric acid are suspected to be present, a considerable quantity of the fluid must be boiled in order to coagulate any albumen that may be present, and must then be filtered and evaporated to one fourth of its original volume. Fluids of this nature are generally of a yellowish colour, may be either clear or turbid, and may or may not contain albumen.

In the examination of the allantoic fluid, crystals of allantoin are gradually formed, which, after being purified by

<sup>1</sup> [Mucin is the peculiar animal matter of mucus; a brief notion of its leading characters is given in the chapter on the "Secretions of Mucous Membranes."]

<sup>2</sup> As chondrin and glutin are not constituents of any of the animal fluids, we have deemed it unnecessary to notice them in the text.

recrystallization, and dissolved in water, cannot be precipitated by acetate of lead, nitrate of silver, or nitrate of the black oxide of mercury.

If the fluid, during evaporation, gives off an urinous odour some hydrochloric acid must be added, and it must be allowed to stand for some time. If acicular crystals are formed, which, after being purified by recrystallization, and dissolved in water containing enough alkali to neutralize the acid of the crystals, give a white precipitate with the above-named tests, an orange with the perchloride of iron, and when moistened with nitric acid, and warmed, do not assume a purple-red colour, they consist of *hippuric acid*.

If however the crystals are very minute, are not readily dissolved in water, and give, when moistened with nitric acid and warmed, a purple-red stain, they are *uric acid* crystals.

4. If the fluid which we are examining is of a brownish yellow colour, and if on treating a little of it with an excess of nitric acid, the colour successively changes to green, blue and red, then biliphæin is present.

5. On evaporating a portion of the fluid to dryness, pulverising it, and boiling it with ether, we obtain, by the evaporation of the ethereal solution, a fatty residue. If it be fluid, it is composed of olein, if it have a tendency to be solid, either stearin or margarin, or both are also present. The fatty acids, and probably free lactic acid, with traces of other substances may be present, especially if the ether contained any alcohol or water. These substances remain in solution, on washing the fatty residue with water. The lactic acid may be easily recognized by its acid reaction; and the fatty acids may be detected by the addition of acetate of lead or acetate of copper to their alcoholic solutions. They are completely precipitated in this manner, and a residue of pure fat is left, which must be again washed and the water removed by evaporation. The fat must then be saponified; if a portion of it resists this process, cholesterin or serolin, or both, must constitute a portion of the fatty residue. They must be taken up by ether, after the saponified portion has been evaporated to dryness. Serolin is less soluble in alcohol, and melts at a lower temperature than cholesterin,<sup>1</sup> by which means the two fats may

<sup>1</sup> [Serolin melts at 95°, cholesterin at about 275°.]

be distinguished. The soaps which have been formed must be decomposed by hydrochloric acid. If, on the addition of the acid, a smell of rancid butter is developed, then butyric, and also capric and caproic acids are present. The variations in their melting points will enable us to determine approximately the proportions of oleic, margaric, and stearic acids.

6. The residue not taken up by ether, must be treated with anhydrous alcohol, which will take up the following substances: salts of the fatty acids, especially soda-salts, as well as any fat that had escaped the action of the ether, also urea, bilin and the acids of the bile, biliverdin, alcohol-extract, hæmaphæin, acetates, and lactates, a class of substances which it is by no means easy to distinguish, and is still more difficult to isolate. If a spirituous solution of chloride of barium be added to the alcoholic solution, and a green precipitate is thrown down, then biliverdin is present; we may also calculate with tolerable certainty (especially if the alcoholic solution has a bitter, bilious taste) on the presence of bilin, and the acids of the bile. An alcoholic solution of sulphuric acid must now be added to the alcohol-solution that we are testing, as long as any sulphates are precipitated. The solution must now be filtered, and the alcohol, which still has an acid reaction if any acetates are present, must be removed by distillation. On treating the residue with water, the fatty acids, if they existed in combination with saline bases, will remain undissolved, and must be removed by filtration. A portion of this watery solution must be evaporated to the consistence of a syrup, and allowed to cool; if, on the addition of an excess of nitric acid, there are formed, either at once or after some time, leafy or stellar crystalline groups, then urea is present. Another portion must be treated with dilute sulphuric acid, and allowed to digest for some time. If bilin, and the products of its metamorphosis, are present, a viscid or oily acid, (insoluble in the acid fluid,) and a precipitate of an extremely unpleasant bitter taste, are formed. The fluid separated from these substances must be digested with pounded marble, or (which is better) with carbonate of baryta, in order to remove the sulphuric acid. It must then be boiled with carbonate of zinc; if it contain lactic acid, crystals of lactate

of zinc will be obtained by evaporation. The extractive matter and hæmaphæin will be left as a residue.

If neither bilin, biliverdin, nor the acids of the bile are present, the investigation may be much simplified. The soda may be separated from the alcoholic solution as a sulphate; we may evaporate, separate the fatty acids by means of water, boil the residue with carbonate of zinc, and filter the solution. By this means we can separate the lactic acid. The urea may be separated from the alcohol-extract by oxalic acid, of which any excess may be removed by digestion with carbonate of lead.

We may be easily convinced of the presence of the alcohol-extract by observing the precipitates which are thrown down by the addition of infusion of galls and a solution of iodine.

The bases, which were present in the alcoholic solution in combination with acids, are now combined with sulphuric acid. They usually are soda and potash.

7. The residue of (6), which was not taken up by absolute alcohol, must now be treated with alcohol of .883, which will take up sugar of milk, diabetic sugar, spirit-extract (which is usually of a brown colour in consequence of the presence of hæmaphæin,) chloride of sodium, phosphates, and probably lactates. If the quantity of sugar (of either of the above kinds) is not very minute, a portion of it will usually crystallize either on the cooling of the spirituous solution or by spontaneous evaporation. The presence of the sugar may, however, be easily recognized by the sweet taste of the spirituous solution after evaporation. If the solution be evaporated to the consistence of an extract, and then treated with cold alcohol of .850, the greater part of the sugar will remain undissolved, while most of the extractive matter will be taken up. The presence of the extractive matter may be determined partly by the brown colour of the spirituous solution, and more decidedly by the precipitates which are caused by the addition of bichloride of mercury, acetate of copper, and tannin. The spirit-extract usually evolves during evaporation a peculiar odour, somewhat resembling that of toasted bread. On evaporating a portion of the spirituous solution to dryness, and incinerating the residue, the ash will be found to consist of chloride of sodium, phosphates, and (if any lactates are present) carbonates of potash and soda. These may be separated in the ordinary manner.



8. The residue not acted on by alcohol of .850 must be dissolved in water, in which, if no protein-compounds are present, it will dissolve without leaving a residue, although the solution may not be clear. In this solution there will be contained pyin, ptyalin, water-extract, phosphates, and perhaps some chloride of sodium. The pyin is recognized by the precipitate afforded by acetic acid. The ptyalin, when it is present only in small quantities, and is mixed with extractive matter, is not easily detected; the only course we can adopt is to precipitate the whole of the extractive matter of the water-extract with the basic acetate of lead. A stream of sulphuretted hydrogen must then be passed through the fluid in order to precipitate the lead. The liquid, after filtration or decantation, must be evaporated to the consistence of a syrup, and the ptyalin precipitated by alcohol.

I may here remark that, in pursuing the directions laid down in (7), we do not succeed in obtaining all the spirit-extract that exists in the residue of (6). Hence in practice it is better to dissolve the residue of (6) in a little water, so as to reduce it to the consistence of a syrup, and then to precipitate with alcohol of .833. The salts may be obtained by incinerating a portion of the evaporated fluid.

In the last six paragraphs we have assumed that no protein-compounds are present. If, however, this should not be the case,—if some of the constituents of the blood, as, for instance, globulin or hæmatin, exist in the fluid, a different course must be pursued. The presence of globulin and hæmatin, and, consequently, of albumen, may be easily ascertained. The fluid must be boiled, evaporated on the water-bath to dryness, and the residue reduced to a fine powder. The fat must be taken up with ether, and the urea, alcohol-extract, bilin, with its acids, and any hæmaphæin and lactates that may be present, with anhydrous alcohol. The residue must be boiled in spirit of .915 until it ceases to communicate any additional red colouring matter to that fluid. In this way we shall obtain the globulin, hæmatin, hæmaphæin, sugar, extractive matters, and several salts, in a state of solution. The greater portion of the globulin and hæmatin is thrown down as the fluid cools; the turbid supernatant fluid is then evaporated on the water-bath to a small residue, and treated with alcohol, which precipitates

the remaining portion of those two constituents. Other substances are contained in the spirituous solution, which may be distinguished and separated by the rules already given.

The residue not taken up by the alcohol of '915 must be treated for some time with water, by which pyin, ptyalin, and water-extract will be taken up. The albumen remains as a residue, usually more or less reddened by a little hæmatin.

If the fluid be very rich in albumen, this course does not succeed, inasmuch as we are unable to obtain a complete separation of those substances which are soluble in dilute alcohol, as sugar, urea, salts, and extractive matters. The following simple modification may in that case be adopted. The protein-compounds must be precipitated by anhydrous alcohol. A spirituous solution is thus obtained, which, even when concentrated, holds the urea, sugar, &c., in solution, while the protein-compounds (at least the albumen) are reduced to an insoluble condition. The coagulated protein-compounds are always mixed up with a certain amount of foreign matters, as, for instance, water-extract, which cannot be easily separated. After the removal of the albumen, &c., the spirituous solution must be evaporated to the consistence of a syrup. On the addition of anhydrous alcohol, sugar, spirit-extract, any albumen that had escaped the former process, and some other substances, will be precipitated. The alcoholic solution must be evaporated, and the residue dissolved in water, by which means the fat will separate itself. The fat is, however, difficult to remove, in consequence of the slow and torpid manner in which the fluid permeates the filter. It is better, therefore, to evaporate the alcoholic solution, at a very gentle temperature, to dryness, and then to take up the fat with pure ether.

In searching for minute quantities of urea in alcoholic solutions of concentrated animal fluids, it frequently happens that, after evaporation of the alcohol, the removal of the fat, and the solution of the residue in water, the action of nitric acid on the urea is much impeded by the presence of compounds of the fatty acids. I therefore usually remove the bases from the alcoholic solution by means of sulphuric acid, which liberates the fatty acids, and allows of their removal with the fat by means of ether. The sulphuric acid should be much diluted with strong alcohol; and as it is of importance that there

be no excess of the acid, it must be added *guttatim*, and only so long as it produces a precipitate, which sometimes is not observed for several hours after the addition of the acid. The effect of the sulphuric acid should first be tried on a small portion of the fluid.

If it is difficult to lay down general rules for the qualitative analysis of all the proximate constituents that can by any possibility occur in the fluids of the animal body, it may easily be conceived that an attempt to lay down similar rules for quantitative analysis would involve much greater difficulties. Such a general quantitative scheme is, however, not required, since quantitative analyses are always preceded by, and based on, qualitative investigations. The fluids most troublesome to analyse are the blood and the urine, on account of the large number of different substances that always occur in them. The rules for the quantitative analysis of the various fluids will be found in the respective chapters on the blood, milk, urine, &c.

## CHAPTER II.

### THE CIRCULATING FLUIDS.

#### *The Blood.*

THE following scheme will explain the arrangement which we have adopted for the general consideration of the blood.

#### 1. *The General Physiological Chemistry of the Blood.*

Its general physiological and chemical relations; the development of the blood-corpuscles; the phenomena of circulation and respiration; the metamorphosis of the blood, and animal heat.

#### 2. *The Special Chemistry of the Blood.*

The method of analysing the blood.

Healthy blood.

Diseased blood.

## 1. The general physiological chemistry of the blood.

*General physical relations of the blood.*

The blood, while moving in the living body, consists principally of a nearly colourless fluid, in which the blood-corpuscles are swimming; in consequence, however, of these corpuscles being too minute to be distinguished by the naked eye, it appears, among the higher classes of animals, as an opaque and intensely red fluid.

In the majority of the lower (invertebrate) animals, the blood is white; it is however red in the annelida, colourless in most of the mollusca, but in many of the snails of a milk-white colour; in the *Helix pomatia* of a sky-blue, and in the *Planorbis corneus*, of a dark amethyst colour. In the dorsal vessels of insects it is usually transparent, and of different colours; it is, for instance, green in the Orthoptera, yellow in the silkworm, orange in the caterpillar of the willow-moth, and of a dark brown colour in most of the beetles.<sup>1</sup> The blood-corpuscles of red blood contain within their coat, or shell, a fluid impregnated with globulin and hæmatin, and a nucleus, which may be easily recognized in the larger corpuscles.

The blood of the mammalia is a somewhat thick, viscid fluid, with a specific gravity which varies, according to different authors, from 1041 to 1082. In a large number of experiments made upon the blood of man, the ox, and the horse, I found it to be between 1051 and 1058. The average was 1042, which corresponds very nearly with the statement of Berzelius.

[The average specific gravity of human blood may be fixed at 1055 according to Nasse,<sup>2</sup> and at 1056 according to Zimmermann.<sup>3</sup> The blood of man is always thicker, and at least one thousandth heavier than that of woman; in a state of health it is always above 1053 in man, while in woman it is frequently not above 1050. Robust men will not unfrequently yield blood of spec. grav. 1058 or even 1059, while in pregnant women the specific gravity is sometimes as low as

<sup>1</sup> Burdach's Physiologie.

<sup>2</sup> Article 'Blut,' in Wagner's Handwörterbuch, vol. 1, p. 82.

<sup>3</sup> Hufeland's Journal, 1843.



1045. In very young infants the blood is thin, and of low specific gravity; according to Denis the blood of the umbilical arteries has a specific gravity of 1075. The specific gravity of the blood of numerous animals has been determined by Dr. J. Davy<sup>1</sup> and by Nasse.]

I found that the blood, as it issues from the aorta, has a temperature of 103° in the ox, and 99°·5 in the pig. Thackray places the temperature of the blood of the horse at 96°·8, of the ox at 99°·5, of the sheep at 101°·3, and of the duck at 105°·8. The temperature is always higher in birds than in the mammalia. The observations of J. Davy, Becquerel, Breschet, Mayer, and Saissy, tend to show that the temperature of arterial is about 1°·8 higher than that of venous blood.

### *Microscopic analysis of the blood.*

If the blood be examined with the microscope (either in a transparent living part, or immediately after its removal from the body), it will be seen to consist of a great number of yellow corpuscles swimming in a colourless fluid. In the higher animals the form of these corpuscles is either circular or elliptic, and invariably flattened.

Under a magnifying power of 300 diameters, they assume the appearance of fig. 1*a* in the blood of man and the mammalia, of fig. 1*b* in the blood of birds, and of fig. 1*c* in the blood of fishes and amphibia. Müller<sup>2</sup> found the greatest degree of flattening in reptiles, amphibia, and fishes. He found that in frogs the thickness does not measure more than one eighth to one tenth of the long diameter, and that in man it measures about one fourth or one fifth of the transverse diameter.

In addition to the blood-corpuscles, lymph-, chyle-, and sometimes oil-globules are present. The first two are round, of a finely granular appearance, and about the size of the blood-corpuscles, from which they may be distinguished by their want of colour, their more perfect sphericity, and their granular appearance.

<sup>1</sup> Anatomical and Physiological Researches, p. 24.

<sup>2</sup> Handbuch der Physiologie des Menschen, vol. 1, p. 105.

These distinctions are sufficient to prevent them from being mistaken for blood-globules. Globules of oil may be immediately recognized by their well-defined dark edge, and by their great refractive power. They do not rotate, and are not granular, but perfectly transparent.

The size of the blood-corpuscles varies in different animals.

In man, the diameter varies, according to Wagner,<sup>1</sup> from  $\cdot0004$  to  $\cdot0002$  of a French inch; according to Müller,<sup>2</sup> from  $\cdot00035$  to  $\cdot00023$ , and according to Schultz<sup>3</sup>, from  $\cdot00036$  to  $\cdot00031$ . The thickness, according to the last observer, may be estimated at  $\cdot000085$  of the same measure. Of all the mammalia, the ruminants seem to possess the smallest blood-globules. Wagner has given the following proportions:

In man and monkeys  $\frac{1}{300}$ th of a line = 3.

Carnivora . . .  $\frac{1}{400}$ th of a line = 4.

Ruminantia . . .  $\frac{1}{500}$ th of a line = 5.

In addition to these admeasurements, the following are deserving of notice: Nasse fixed their average diameter at  $\cdot00033$ , the maxima and minima being  $\cdot00036$  and  $\cdot0003$ ; Bowerbank places their average diameter at from  $\cdot00035$  to  $\cdot00027$ , the extreme limits being  $\cdot00054$  and  $\cdot00021$  respectively; Owen at  $\cdot00028$ ; and Gulliver at  $\cdot0003$  of an inch.

The dimensions of the blood-corpuscles in the following animals have been measured:

Ape (*Simia callitrix*)  $\cdot00037^4$  (Prevost and Dumas).

Cat  $\cdot00028$ ; dog  $\cdot00031$  (Schultz); rat and mouse about  $\cdot00025$  (Wagner).

Sheep  $\cdot0002$  (Schultz and Wagner); ox  $\cdot0002$  (Schultz) and  $\cdot00024$  (Wagner); goat  $\cdot00017$ ; chamois  $\cdot0002$  (Prevost and Dumas); horse  $\cdot00031$ — $\cdot00027$  (Schultz). According to Wagner, the diameter in rats, mice, hares, and squirrels, varies from  $\cdot00025$  to  $\cdot00020$ .

The blood-corpuscles of birds, fishes, and amphibia are elliptical. The following are the results of some of the best authenticated measurements:

Common fowl: length  $\cdot00062$ ; breadth  $\cdot00036$ ; thickness  $\cdot00013$  (Schultz). According to Dumas and Prevost, the long

<sup>1</sup> Nachträge zur Physiologie des Blutes, 1838, p. 5.

<sup>2</sup> Physiologie des Menschen, vol. 1, p. 106.

<sup>3</sup> System der Cirkulation, p. 14.

<sup>4</sup> French inches.

diameter in the pigeon, duck, and goose, varies from  $\cdot0008$  to  $\cdot00044$ ; the short diameter from  $\cdot0004$  to  $\cdot00029$ . Wagner estimates the two diameters, in the pigeon, at  $\cdot0008$  and  $\cdot00033$  respectively.

We find the largest blood-corpuscles in fishes. According to Wagner<sup>1</sup> the largest corpuscles, at present observed, are those of the torpedo, their long diameter being  $\cdot002$ ; in the skate he found them to vary from  $\cdot001$  to  $\cdot0012$  in length; in the loach the long diameter was  $\cdot0005$ ; in the eel-pout,  $\cdot00057$ ; in the barbel  $\cdot00066$ , the short diameter in this case being  $\cdot0004$ .

In the carp the long diameter is  $\cdot0005$ , and the nucleus measures  $\cdot00012$ .

In the plaice, Schultz estimated the long and short diameters at  $\cdot00062$ , and  $\cdot00043$  respectively, and the thickness at  $\cdot00007$ .

In the naked amphibia the corpuscles are very large. In the triton, Dumas and Prevost estimated the diameters at  $\cdot00128$  and  $\cdot00078$  respectively. In the *Salamandra cristata*, Schultz found that the diameters were  $\cdot00138$  and  $\cdot000804$  and that the thickness was  $\cdot000315$ . In the frog, the same observer estimated the length, breadth, and thickness at  $\cdot00108$ , and  $\cdot00058$ , and  $\cdot000017$ .

Of all the amphibia, the water-snakes appear to possess the smallest blood-corpuscles.<sup>2</sup>

The instantaneous effect of water upon the blood-corpuscles is very remarkable, and is easily seen under the microscope: they swell, become globular, lose their distinct contour, and (if much water be added,) altogether disappear. If however the blood-corpuscles have nuclei of sufficient magnitude to admit of examination (as in the blood of fishes, reptiles, &c.), these nuclei will be seen swimming in the water after the disappearance of the capsules.

The nuclei may be separated in a similar manner, by the addition of a little acetic acid. The acid in a few minutes dissolves the hæmato-globulin, and assumes a yellow colour.

<sup>1</sup> Zur vergleichenden Physiologie des Blutes, 1833, p. 14. [The largest blood-corpuscles do not occur in fishes, as stated in the text, but in some of the naked amphibia. See Wagner's Physiology, p. 236, English edition.]

<sup>2</sup> A very complete account of the sizes of the blood-corpuscles of different animals, as far as they had been then ascertained, may be found in Wagner's Nachträge zur Physiologie des Blutes, 1839, p. 31.

If, upon the addition of water, the blood-corpuscles have swelled to such a degree as to be imperceptible under the microscope, they may be restored to their pristine form by the addition of a solution of sugar, of common salt, of nitrate of potash, or of muriate of ammonia. Schultz<sup>1</sup> explains this phenomenon by the supposition that the capsule of the blood-corpuscle is an organic structure, which is stimulated to contraction by the above solutions, but which is relaxed or expanded by water. In confirmation of this view, he observes that the hæmato-globulin is not precipitated by the action of the sugar or salts. Schultz has also shown that when the capsules have even fallen to pieces in the water, the addition of a little tincture of iodine, diluted with water, will render their fragments visible.

The blood-corpuscles do not always present a regular nummular and flattened appearance; they are sometimes plicated and bent in.

The cause of this phenomenon is not known, but it is probably due to a contraction of the capsule at different points. One of the most peculiar of these forms is that in which the edge of the blood-corpuscle appears as if it were studded with minute pearls. In the blood of a patient suffering from Bright's disease, I found that nearly all the corpuscles had undergone this modification. On the addition of a solution of muriate of ammonia, the appearance it presented under the microscope was very striking. I immediately made a counter-experiment with my own blood, but it did not exhibit the phenomenon in question.

Ascherson<sup>2</sup> has offered the following explanation of this peculiarity in the form of the corpuscle, viz., that it is due to the exudation of fat which exists in a fluid state in the blood-corpuscle.

In opposition to this view, it may be urged, that if each individual corpuscle contained a separable portion of fat (however minute it might be), we should obtain in our analyses a much larger quantity of fat than in reality we do. It is true that the dried clot yields a larger proportion of fat than an equal

<sup>1</sup> Ueber die gehemmte und gesteigerte Auflösung der verbrauchten Blutbläschen. Hufeland's Journal, April 1838, p. 18.

<sup>2</sup> Müller's Archiv, 1840. Ueber die Bedeutung der Fettstoffe.



weight of serum, but the difference is by no means so striking as it would have been if Ascherson's theory were correct.

Hünefeld<sup>1</sup> has observed a similar appearance on treating the blood-corpuscles of the frog with putrid serum, in which granules were present. The granules seemed to form a sort of girdle round the corpuscle, and he conceives that they penetrated into minute depressions upon the surface of the capsule. If this statement be correct, it is strongly opposed to the observations of Ascherson and Wagner respecting the lubricity and evenness of the blood-corpuscles.

On mixing the blood of a carp with a solution of sugar, and on the cautious addition of water, I observed that the blood-corpuscles assumed a stellar appearance.

On treating frog's blood with bilin, an agent which usually dissolves the corpuscles, I observed that some of them resisted this action for a considerable period, and ultimately assumed a pyriform appearance, while others became narrowed at the centre, and extended at both extremities. Others, again, seemed to undergo an internal change, and appeared as if their inner surface were studded with minute vesicles.

Hünefeld made a similar observation on treating frog's blood with carbonate of ammonia.<sup>2</sup>

The same chemist observed a remarkable peculiarity in the corpuscles of human blood, on the addition of sulphate of quinine. In the course of a few minutes they assumed an irregular, angular form, and appeared as if their sides were drawn together.

Schultz<sup>3</sup> has made the following important microscopic observation. On examining the blood-corpuscles of a salamander which had been suffocated in carbonic acid gas, they were found to be of a darker colour than usual; the darkness was particularly marked on some spots, so that they exhibited a sort of chequered appearance.

On shaking the blood with oxygen gas, the corpuscles became brighter and more transparent.

<sup>1</sup> *Der Chemismus in der thierischen Organisation*, p. 101.

<sup>2</sup> *L. c.*, p. 106.

<sup>3</sup> *System der Cirkulation*, p. 27.

*A. The general chemical relations of the blood.*

The general chemical relations of the blood-corpuscles.

Müller and Schultz have examined the action of various tests on the blood-corpuscles. Hünefeld<sup>1</sup> has also recently paid much attention to the apparent effect produced on them by numerous medicinal agents. According to the last-named author, the corpuscles and their nuclei are soluble in the following substances: caustic ammonia, potash, soda, lime, and baryta, soap, bile, acetic acid, hydrocyanic acid, alcohol, ether, oil of turpentine, ethereal oil, and sulphuret of carbon.

The capsules, but not the nuclei, are soluble in water, in all the salts of ammonia, the carbonates of potash and soda, cyanate of potash, borax, chloride of barium, chloride of calcium, the salts of oxalic and hydrochloric acids, concentrated vinegar, and the phosphoric, arsenic, oxalic, citric, and hydrochloric acids.

Phosphorus, chlorine, and iodine produce a similar effect, probably by the formation of an acid.

An imperfect solution is effected by flowers of sulphur, tartrate of ammonia, borate of ammonia, bromide of potassium, and malic acid.

The corpuscles are not dissolved by carbonate of magnesia, veratrine, strychnine, acetate of morphine, hydrochlorate of concine, boracic acid, carbonic acid, nitrate of potash, nitrate of soda, tartrate of soda, phosphate of soda, chloride of sodium, sugar, gum, sulphate of potash, sulphate of magnesia, sulphate of soda, tartar emetic, camphor, anemonine.

Hünefeld also tried the effects of several of the animal fluids on the blood. Saliva, phthisical sputa, and healthy pus produced no well-marked changes. Gastric juice, added to an excess of blood, induced a slight coagulation, and changed the red colour into a brown. The extractive matter of the flesh of rabbits and calves produced no change on the corpuscles, but the colour assumed a more vermilion tint, and the corpuscles sank sooner than usual. Acid whey, concentrated by evaporation, produced no effect, neither did the pancreatic juice or gonorrhoeal discharge. Sweat, taken from the axilla, changed the colour to a lighter red, and, in the course of some hours,

<sup>1</sup> Der Chemismus, u. s. w., p. 43-84.

dissolved the corpuscles, (possibly through the influence of the ammoniacal salts.)

Pure urea, prepared artificially, induced no change in the colour, but dissolved the corpuscles, with the exception of the nuclei and a few fragments of the capsules.

The action of putrid blood and serum has been already noticed.

Human blood does not appear to be influenced by admixture with the blood of birds or frogs.

The bile of man, quadrupeds, birds, fishes, and amphibia, exerts an active soluble influence upon the corpuscles. In some observations on frog's blood, Hünefeld noticed that the capsules were immediately dissolved, and that the nuclei remained unchanged for some time, but ultimately broke up into minute granules and disappeared.

The effects produced by concia appear, from Hünefeld's observation, to be very singular.

Conceine, either in a state of solution or vapour, reduces the blood to a dirty red greasy mass, which, under the microscope, resembles dark melted wax, and in which no corpuscles can be detected. If diluted blood be treated with a little conceine, it remains fluid, but, after a short time, becomes discoloured, and throws down a brown sediment. The blood of a rabbit, poisoned with conceine, exhibited no peculiarity.

Arsenic acid produces no material effect upon the blood, nor could Hünefeld detect any alteration in the corpuscles of a frog destroyed by this agent.

On passing hydrocyanic acid, in a state of vapour, into the blood of a pig, the colour became more vivid, and the corpuscles remained uninjured for a very considerable time. A large quantity of blood, which was treated in a similar manner, gave off a strong odour of the acid after the lapse of a year and a half, and did not exhibit any symptoms of putrefaction. No change could be observed in the blood of a rabbit poisoned with this agent.

Chlorate of potash does not produce any apparent effect for the first few minutes; subsequently, however, the blood assumes a brighter red tint, which ultimately passes into a brown. An ounce of fresh human blood was mixed with eight grains of chlorate of potash. Just at first the colour became rather

brighter, but, after the lapse of from fifteen minutes to an hour, it became darker than it previously was. It then became of a reddish brown colour, and, after from eight to sixteen hours, it was converted into a pulpy brownish-black matter. The blood of a cat which had taken a drachm of this salt, and had afterwards been killed with cyanogen, exhibited no peculiar appearance.

Hünefeld, and some other microscopists, assert that acetic acid dissolves the whole of the corpuscle, with the exception of the nucleus. Müller, on the contrary, maintains that in frog's blood the colouring envelope is not wholly dissolved, but may still be frequently observed in a pale fine line surrounding the nucleus.

The following are my own observations with respect to this test. If a sufficient quantity of acetic acid be added to freshly drawn blood, so as to give it a decidedly acid reaction, and if the vessel in which it is contained be submitted to a temperature of about  $88^{\circ}$  for half an hour, the blood becomes changed into a thick tar-like mass of a blackish brown colour.

If water be now added, and the mixture carefully stirred until it is reduced to a magma of an equal consistence throughout, we find that, on examining a portion of this mixture under the microscope, the addition of some more water does not dissolve the corpuscles; in fact, they are no longer soluble in water, in consequence of the insoluble compound that has been formed by the acetic acid, and the (casein-like) globulin. If a great excess of water be added, the corpuscles sink; the albumen, and a great portion of the hæmatin, which enter into their composition, are dissolved, and they become almost perfectly clear. They may even be boiled in water, without any change in their form being produced.

When boiled in acetic acid (unless it be very dilute), they become perfectly dissolved, with the exception of their nuclei.<sup>1</sup>

According to Müller and Schultz, a solution of caustic ammonia dissolves the corpuscles more rapidly than a similar solution of caustic potash. The same observers state that alcohol does not dissolve them, but merely produces a slight contraction or puckering, and that the granules of albumen

<sup>1</sup> F. Simon's Beiträge zur Kenntniss des Blutes, in Brandes's Archiv, vol. 18, p. 35.



coagulated by this reagent cloud the field of vision, and render the corpuscles indistinct. I have also found that neither absolute alcohol, nor alcohol of  $\cdot 835$ , effect the solution of the corpuscles.

It has been found by Schultz, Hünefeld, and myself, that the blood-corpuscles dissolve upon the addition of a small quantity of ether. A quantity corresponding in volume to from one third to one half of the blood is perfectly sufficient. This experiment has been successfully repeated upon the blood of man, the ox, the frog, and the carp.

If the experiment be performed in a test-glass, it will be observed that the colour of the blood very soon becomes deepened, but that ultimately the whole fluid becomes transparent. The ether does not separate during this process.

If a portion of this mixture be covered with a slip of thin glass, and examined under the microscope, no corpuscles, but simply the nuclei, are discernible. The nuclei in the blood of man and the ox cannot be clearly seen on account of the colouring matter that is always present ; they may, however, be always distinctly observed in the blood of the frog or the carp for a considerable time.

A mixture of ether and blood, kept in a stoppered vessel for some time, became thick, assumed a greasy appearance, and was no longer fit for the experiment ; neither could a satisfactory result be obtained on shaking blood with an excess of ether ; for then the ether took up the water of the blood, and thus reduced that fluid to a state of thickness.

On pouring off the ether from a known quantity of blood with which it had been continuously stirred for twenty-four hours, and submitting the blood to a single washing with ether, I was astonished to find that from the two ethereal solutions I obtained quite as large a quantity of fat as I should have done by the repeated extraction of a corresponding portion of dried and finely-powdered blood with boiling ether. On treating pure liquid serum of the same blood in a similar manner, the quantity of fat obtained did not differ from the quantity obtained from the perfect blood, in a ratio sufficient to justify the supposition, that the capsules are composed of fat.

I can also confirm Hünefeld's observation respecting the influence of bile upon the blood. On the addition of fresh bile,

the blood immediately becomes clear, and the corpuscles disappear. In consequence of the viscosity of ordinary bile, I experimented with pure bilin.

Upon the addition of a little partially dried bilin to the blood of man, the calf, the tench, or the frog, the fluid becomes, after a little stirring, thick, almost gelatinous, capable of being drawn out into threads, and no corpuscles can be seen in it. If a minute drop of frog's blood, in which the corpuscles have been thus dissolved, be brought in contact, and suffered to mix with a fresh drop of blood from the same animal, an interesting microscopic object is afforded. After the first intense action is over, the corpuscles are seen to move about slowly, or to be in a state of rest, and gradually to disappear. The solution of the capsule (not of the nucleus) occurs so instantaneously that the eye cannot trace the reaction. The nucleus always remains as a granular mulberry-like corpuscle. It becomes gradually paler and paler, enlarging itself visibly at the same time, and at last its existence can only be ascertained by its brightness. I have never succeeded in observing the decomposition of the nucleus into its constituent parts, which has been described by Hünefeld, although I have carefully repeated his experiments. I usually observed, however, that at those points where many corpuscles had disappeared, numerous minute points were visible, of which the larger ones displayed a lively molecular motion. In those instances in which the corpuscles resisted the solvent power of the bilin for a considerable time (possibly in consequence of the reagent being applied in too dilute a state), they often assumed very peculiar forms; appearing as if they were twisted, and extended longitudinally in one direction, or variously coloured in the interior. (Vide *supra*, p. 106.)

I have formerly noticed the solvent power of olive oil upon the corpuscles.<sup>1</sup> I shook a quantity of the blood of a calf, which had been allowed to flow from the vein into a vessel one quarter full of olive oil, until the blood was perfectly cool. No corpuscles could then be detected. Whipt blood exhibits the same phenomenon; but in this case it is requisite that the oil should remain for a longer period in contact with the blood. This fact has also been noticed by Magendie.<sup>2</sup>

<sup>1</sup> Pharmaceutisches Centralblatt, 1839, p. 672.

<sup>2</sup> Leçons sur le Sang, et les alterations de cet liquide, par Magendie. Bruxelles, 1839. p. 244.

B. *The general chemical relations of the colouring matter of the blood (Hæmatin.)*

The red colouring matter of the blood is contained, in all probability, in a state of solution in the corpuscles, an opinion which is also supported by Müller, Schultz, and Reichert. If, in the examination of frog's blood, one corpuscle be observed to move over another, the lower can be distinctly perceived through the upper one. Moreover, the instantaneous solution of the corpuscles by means of bilin supports this view; for, if their contents were gelatinous or solid, the act of solution would be observed to progress from the circumference to the centre, and would admit of being observed by the microscope.

Hünefeld<sup>1</sup> seems to support the opinion that the colouring matter exists in an insoluble form, attached to the inner surface of the capsules. If, however, this were the case, the blood-corpuscles would appear more opaque than they do. The observations of Hünefeld and others show that the following substances heighten the red colour of the blood: cold water-extract of the flesh of rabbits and calves (having an acid reaction) communicates a vermilion colour to the blood. It becomes of a deep garnet red by the carbonate, cyanate, and nitrate of ammonia, and less intensely by the saliva, phthysical sputa, gonorrhœal matter, sweat, hydrocyanic acid, the carbonates of soda and potash, and bicarbonate of soda.

A brown tinge may be produced by the agency of several substances; for instance, by all free acids, by sugar of milk, oil of bitter almonds, ammonia, boracic acid, carbonate of magnesia, tartrate of potash, bromide of potassium, sulphate of magnesia, chloride of strontium, nitrate of strontia, lactate of iron, phosphorus, iodine, &c.

The alkalis, alkaline earths, and sulphuret of potassium produce a green tint. It becomes entirely decolorized by the action of coneine and oil of turpentine.

c. *The general chemical relations of the nuclei of the blood-corpuscles.*

The similarity of the constitution of the nuclei to coagulated fibrin has been long observed. Hünefeld,<sup>2</sup> however, conceives

<sup>1</sup> L. c., p. 104.

<sup>2</sup> Der Chemismus, u. s. w., p. 108.

that corpuscles, instead of consisting of fibrin, are mainly composed of fatty matter (either cholesterin or some allied substance), combined with albumen, as occurs in the yolk of eggs. In this view I cannot coincide, although I fully believe that albumen and fat do take a very active part in the formation of all the animal tissues, and, consequently, in the production of the blood-corpuscles. In this instance, the formative process has advanced so far that we can expect to find the original materials of formation present in only very small quantities. It is true that the fibrin and the blood-corpuscles contain a greater relative proportion of fat than the other constituents of the blood; yet even in fibrin the proportion amounts to only 5%, and the fat cannot therefore be regarded as a preponderating constituent of this substance. That the fat is not actually cholesterin seems pretty clear from the fact of the ready solubility of the corpuscles in caustic potash.

The diameter of the nucleus is usually about one-fourth or one-fifth of the diameter of the blood-corpuscle. In the amphibia it varies from .002 to .005; in fishes, from .0016 to .0025; in birds, its length is about .002, and in the mammalia .0008 of a line.

I have made the following observations with regard to the nuclei in the blood of man,<sup>1</sup> the carp, and the frog. The nuclei in the frog appear, after the solution of the capsule and hæmato-globulin, as partly elliptical and partly cylindrical. After washing them for a day or two in order to remove the colouring matter and albumen, they assume a more spherical form, and most of them present a granulated appearance on the surface. I cannot, however, positively assert that granular cells were present, nor did I observe the nuclei separate into distinct portions during this treatment. The nuclei, even when moist, were not soluble in boiling ether. When dried, moistened with water, and then observed under the microscope, several nuclei were seen floating about, apparently unaltered; many were, however, connected together in such a manner as to prevent their whole outline from being apparent. Upon treating the dry nuclei with ether, appearances similar

<sup>1</sup> I allude to the nearly colourless sediment which may be obtained by washing blood with a large quantity of water, and which is found to contain lymph-corpuscles and fragments of capsules.



to those already described were perceived. Moist nuclei dissolved readily in caustic potash; if the solution be supersaturated with concentrated acetic acid, and heated, an imperfect solution of the matter, precipitated by the acid, occurs; a very small quantity of dilute hydrochloric acid will, however, readily dissolve the whole. On treating the filtered solution with tannin, a copious precipitate was thrown down; ferrocyanide of potassium caused a mere turbidity, or very slight deposit. Similar observations were made on the nuclei of carp's blood, but the ferrocyanide of potassium caused less turbidity than in the former case. The nuclei of human blood are scarcely discernible in the viscid sediment. The effect of reagents was much the same as in the former cases.

Hence we are led to infer that the blood-corpuscles are chiefly formed of a substance closely related to the protein-compounds, although not identical with any of them: possibly the nuclei may be converted into fibrin, soluble in the liquor sanguinis, after the metamorphosis of the blood-corpuscles has been accomplished. On heating the nuclei on platina foil, a fatty smell is first observed, and then an odour resembling that of burning albumen. Upon heating them in a test-tube, and applying litmus paper, the red colour is soon changed to a strongly-marked blue. The ash has a reddish appearance, and consists of peroxide of iron, lime, and phosphoric acid.

D. *The general chemical relations of the plasma (liquor sanguinis).*

The plasma of living blood exists as a clear fluid, in which the corpuscles are seen to float. If the blood has been removed for some time from the body, the fibrin separates from the plasma. This separation appears to take place simultaneously and uniformly throughout the whole of the blood. As the fibrin contracts, it entangles the corpuscles; the subsequent contraction tends to expel the serum, and thus the clot is produced. The clot, at first soft and gelatinous, becomes gradually more consistent, and ultimately appears as a mass, capable of a certain degree of resistance, and floating in the serum.

There are certain pathological conditions, under which the

blood cannot hold the corpuscles in suspension. There is then formed, previously to the separation of the fibrin, a layer of yellow plasma above the sunken blood-corpuscles, in which (i. e. in the plasma), upon the subsequent coagulation, a certain quantity of fibrin separates (*crusta inflammatoria*).

In some observations on the blood of a cachectic horse, made during the summer, I found that the corpuscles sunk so rapidly in the tumbler in which the fluid was received, that a layer of plasma was formed, amounting to nearly two thirds of the whole volume of the blood, previously to the coagulation of the fibrin. The fibrin, which was present in large quantity, then began to coagulate, and after some time a solid cylinder of coagulated plasma was formed, which resisted a considerable degree of pressure, and under which the uncoagulated blood-corpuscles were distributed.

In some pathological states the blood contains mere traces of fibrin; in these cases no clot is formed; we observe merely the separation of a few dark gelatiniform flocculi.

The coagulation of the plasma is a consequence of the cessation of the vitality of the blood; hence it occurs not merely in blood abstracted from the living body, but after death, and under some peculiar circumstances, in the vessels themselves. It is independent of external influences, for it occurs equally in ordinary air, *in vacuo*, and in various gaseous atmospheres. It may be accelerated or impeded by certain agents, and may even be altogether prevented; the blood, however, when prevented from coagulating in this manner, is in a state very different from that in which it previously existed in the body, the fibrin having undergone a chemical change.

### *The retardation or prevention of coagulation.*<sup>1</sup>

Fresh blood becomes solid below 32°, without the coagulation of the fibrin, which however occurs after thawing.

<sup>1</sup> [A full account of the various experiments by John Hunter, Davy, Prater, Scudamore, and others, on the effects of various agents upon the coagulation of the blood, to the period it was written, may be found in Ancell's seventh lecture "on the Physiology and Pathology of the Blood." *Lancet*, 1840.]

The blood of frozen and apparently dead frogs remains fluid, and the same is the case in hibernating animals, in which the temperature of the blood is reduced to that of cold-blooded animals.<sup>1</sup>

The coagulation of the blood is retarded by contact with animal membranes; it will remain fluid in tied arteries for the space of three hours. Blood which has been infused into the cellular tissue will remain fluid for weeks. Schultz has observed that blood which has collected in the intestines remains fluid for a long time; moreover, the blood which has been abstracted by leeches does not coagulate, as long as it remains in the body of the animal.<sup>2</sup>

Gerhard, Hufeland, and Kichmeyer have shown that blood through which an electric current is continuously passed remains fluid for a long time. Schubeler also showed that positive electricity hinders the coagulation of the blood; moreover, the blood of animals killed by electricity or lightning does not coagulate.

The following salts hinder the coagulation of the fibrin, according to Hewson,<sup>3</sup> Schultz,<sup>4</sup> and Hamburger's<sup>5</sup> observations: sulphate of soda, chloride of sodium, nitrate of potash, chloride of potassium, acetate of potash, and borax, if they be added in the proportion of half an ounce to six ounces of blood. If however the blood be diluted with double the quantity of water, the fibrin coagulates. (Hewson.) The carbonates and acetates prevent the coagulation of the blood, in all degrees of concentration. With regard to the action of the sulphates, a concentrated solution appears to retard the coagulation; a dilute solution, on the contrary, to accelerate it. (Hamburger.) The same appears to be the case with respect to the tartrates and borates.

The following metallic salts impede the coagulation of the fibrin: sulphate of copper, ammoniaco-sulphate of copper, sulphate of the protoxide of iron, chloride of iron, ferrocyanide

<sup>1</sup> Schultz, *op. cit.* p. 80.

<sup>2</sup> L. c., pp. 64 and 81.

<sup>3</sup> *Disquisitio experimentalis de sanguinis natura.* L. B. 1785.

<sup>4</sup> *Op. cit.*

<sup>5</sup> *Experimentorum circa sanguinis coagulationem specimen primum diss. inaug. auct. Hamburger.* Berolini, 1839.

of potassium, acetate of lead, and tartrate of antimony and potash.<sup>1</sup>

Magendie's<sup>2</sup> observations differ considerably from the above. He arranges in a tabular form<sup>3</sup> the following salts which tend to impede the coagulation of the blood: the alkaline carbonates, nitrate of potash, and nitrate of lime. All observers agree that the free alkalies completely prevent the coagulation.

The observations of Schultz, Magendie, and Hamburger show that dilute mineral and vegetable acids prevent the coagulation of the blood, which however thickens, and assumes a syrupy or oily appearance. These statements have been confirmed by myself.

The following non-mineral reagents have been observed by Magendie to prevent or impede the coagulation of the fibrin: nitrate of strychnine, nitrate of morphine, and nicotine. This statement, as far as regards the nitrate of strychnine, has been denied by Hamburger.<sup>3</sup>

Hunter observed that the coagulation was retarded by the addition of a solution of opium, a statement however which is not confirmed by Hamburger. The latter observer notices the effect which is produced by the addition of bile, in preventing the coagulation.

#### *Acceleration of the coagulation.*

The coagulation of the fibrin is accelerated, or at any rate not impeded, by a temperature higher than that of the living blood. According to Hewson, it takes place most rapidly at from 114° to 120°. Scudamore and Schröder van der Kolk assert that the coagulation is accelerated by electricity and galvanic currents, which however is opposed to the previous observations of Kiemeier and others. Contact with atmospheric air hastens the coagulation.

According to Hamburger, no influence, either in accele-

<sup>1</sup> Schultz remarked that hydrochlorate of ammonia, sulphate of potash, and sulphate of magnesia, retain the blood in a state of fluidity, and that even the addition of a large quantity of water does not produce coagulation. After the addition of sulphate of soda, the blood could only be prevented from gelatinising by constant stirring, a step that was not requisite with the other salts.

<sup>2</sup> Leçons sur le Sang. Bruxelles, 1839.

<sup>3</sup> Op. cit. p. 249.

<sup>3</sup> Ib. p. 45.



rating or impeding the coagulation, is exerted by sulphate of lime, chlorate of potash, or iodide of iron.<sup>1</sup>

According to Magendie and Hamburger, the coagulation is accelerated by acetate of morphine. The former observer states that water, a watery solution of sugar, the fluid of dropsy, Seidlitz and Vichy waters, alcohol, ether, and mannite; and the latter, that decoctions of digitalis, and tobacco, solution of tannin, iodine, solution of sugar, gum arabic, starch, and fresh urine, have a similar effect.<sup>2</sup>

#### ON THE CHEMICAL PHYSIOLOGY OF THE BLOOD.

##### *On the formation of the blood.*

The formation of the blood, and especially of the blood-corpuscles, has been made a subject of careful and laborious research by many of the best microscopic observers of the present age, amongst whom we may enumerate the names of Schultz, Baumgärtner, Valentin, Reichert, Wagner, and Schwann.

[As the physiological details connected with this subject belong strictly to the physiology rather than to the chemistry of the blood, we shall content ourselves with a brief statement of all that is known with any degree of certainty regarding this obscure and intricate process.

Capillary vessels are developed by the stellated union of a certain set of blastodermic or germinal cells; and no sooner are capillary or other vessels formed, than a kind of blood is found in them. The corpuscles of that blood differ from those of the adult in being considerably larger, more spherical and granular, and in containing a distinct nucleus. There is probably an external envelope. The granules unite or amalgamate, so as to form the coloured or clear part of the blood-corpuscle, while the nucleus remains. See fig. 2.]

Although much light has recently been thrown on the formation of the blood-corpuscle in the embryo, we are still

<sup>1</sup> Magendie observed that the coagulation is hastened by the addition of the chlorides of potassium, sodium, ammonium, and barium; of bicarbonate of soda, sulphate of magnesia, borax, nitrate of silver, iodide of potassium, and the cyanides of gold and mercury.

<sup>2</sup> [A summary of Mr. Blake's experiments on the effects of various salts, &c. on the blood, is given in Williams's Principles of Medicine, page 99.]

unfortunately almost entirely deficient in positive information regarding the formation of the blood-corpuscles in the mature individual. That blood-corpuscles are formed in adults, cannot admit of a doubt; for we see that the mass of the blood, and consequently of the blood-corpuscles, is continually increasing from the moment that blood is first produced in the embryo, up to the period of full corporeal development. Moreover, independently of any considerations founded on the increased mass of the blood, a continuous formation of blood-corpuscles is obviously necessary to compensate for the waste and consumption of blood dependent on the exercise of the vital functions. The immense quantities of extractive matters (abounding in nitrogen and carbon),—of urea, uric acid, bile, mucus, and fat, which are daily secreted in the urine, faeces, and mucous discharges, together with the considerable amount of carbon which is given off as carbonic acid in the process of respiration,—must all be refunded to the system by the blood. To this it may be objected, that the supply takes place on the part of the plasma, which alone therefore would require to exist in a state of continuous increase, while the corpuscles coexist, and are coeval with the individual in whose blood they occur. Such a view is, however, at variance with all the phenomena of the higher stages of existence; for no tissue or portion of the body, solid or fluid, is allowed to remain unchanged or unendowed with vitality. The necessity for the consumption and reproduction of the blood-corpuscles has never yet been disputed, but various theories have been propounded by different physiologists regarding the seat of their formation and their mode of organic development or metamorphosis.

Hewson endeavours to show that the spleen is the principal organ in which the blood-corpuscles are formed, and that they are produced from lymph-granules. Although the functions of the spleen are not even at the present day properly determined, it is an established fact that the spleen may be extirpated, and the formation of blood not be impeded; moreover, the red colour of the lymph, upon which Hewson strengthens his opinion, has not always been observed.<sup>1</sup> Schultz<sup>2</sup> con-

<sup>1</sup> J. Müller's *Handbuch der Physiologie*, vol. 1, p. 573.

<sup>2</sup> *System der Cirkulation*, p. 37.

siders that the blood-corpuscles are formed in the lymphatic glands, and conveyed by the ductus thoracicus into the blood. He states that the chyle which is found in the vessels issuing from the glands, contains clear, round, oily vesicles, and granular lymph-corpuscles. The diameter of the granular lymph-corpuscles in horses and rabbits varies from  $\cdot 0005$  to  $\cdot 0008$  of a line; and they are so similar to the nuclei of the blood-corpuscles, as to render it very probable that the latter are derived from them. In the lymph of the ductus thoracicus of rabbits and horses, we find actual blood-corpuscles, as well as the transparent and granular lymph-corpuscles; these blood-corpuscles, however, possess more tender, and not perfectly flattened capsules, and a much smaller amount of colouring matter than when they have arrived at maturity. They are consequently paler and more transparent than at a subsequent period, and the nucleus may be inclosed more or less closely in the capsule. The lymph-corpuscles and the nuclei of the blood-corpuscles present a very close analogy, for they both vary in size, and, to use Schultz's own words, "it cannot be doubted that the blood-corpuscles are produced by the formation of a coloured capsule around the lymph-globules."<sup>1</sup>

These blood-corpuscles could not have been transmitted there by blood-vessels; their difference from the mature corpuscle, and their slight amount of colouring matter, are opposed to such a supposition. Since lymph-corpuscles also pass into the blood, the formation of blood-corpuscles from them in the blood-vessels cannot be denied; it may however happen that they are again conducted by the blood to the lymphatic glands, where their metamorphosis is completed. In a more recent work on the Blood,<sup>2</sup> Schultz states that the coloured capsule of the blood-corpuscle is principally formed in the process of respiration. There is much in favour of this view, for we know that the blood can only obtain its nutriment through the ductus thoracicus, and it seems obvious that the conditions necessary for the formation of the blood-corpuscles must be associated with the circumstance of the derivation of the nutriment from this source. Moreover, there can be no doubt that in conse-

<sup>1</sup> L. c., p. 45.

<sup>2</sup> Ueber die gehemmte Auflösung und Ausscheidung der verbrauchten Blutbläschen. Hufeland's Journal, April 1838.

quence of the continuous supply of chyle which is afforded to the blood, the lymph-corpuscles would speedily predominate, unless they underwent some metamorphosis, and assumed another form ; but in reality the number of lymph-corpuscles in the blood is comparatively small. Although the lymphatic glands may be regarded as in some degree the seat of formation of the blood-corpuscles, it must by no means be supposed that the latter issue from these glands in a perfectly developed state ; their ultimate maturity is obtained in the blood, and they aid in the support of its independent vitality. Henle, who likewise coincides in the view just given, as I know from a personal communication with him, has minutely studied the formation of the blood-corpuscle from the lymph-corpuscle, and the transitions of the latter to a state of maturity. He regards the lymphatic glands as the chief, although not the exclusive seat of formation of the blood-corpuscles. Although the chyle does not contain a sufficient number of matured blood-corpuscles to allow us to recognize their presence by its external appearance, we must remember that during its continuous discharge into the subclavian vein, a considerable number of blood-corpuscles may in a certain time be conveyed into the blood : that the blood-corpuscles which are contained in the chyle are formed in the organs of chyfication, and are not conveyed thither by arteries or veins, is clear from our knowledge of the connexions between the vascular and capillary systems.

It is pretty generally allowed that the process of respiration is essentially requisite for the further development of the young blood-corpuscles, after their formation in the lymphatic glands. J. Müller, in his chapter on the formation of the blood, expresses himself to the effect that the contents of the lymphatics, namely the clear lymph and the whitish chyle, are the materials for the formation of the blood, and that this formation is carried on not in any one particular organ, but under the combined influence of the vital functions generally. This view corresponds with the former, if in the materials for the formation of the blood we understand the young blood-corpuscles, (i. e. the lymph- and chyle-corpuscles which are to be changed into blood-corpuscles,) and the plasma, which is still almost destitute of fibrin. If, however, the lymph- and chyle-corpuscles are regarded as having no connexion with the



genesis of the blood-corpuscles, then it is distinct from the previous views. Reichert in his work on Development, has said nothing respecting the formation of blood-corpuscles in the adult; but from a personal communication, I find that he regards the liver as the blood-preparing organ in adults, and the preparation of the blood as the principal function of that gland; the secretion of bile must then be regarded as a consequence of the metamorphosis that occurs during the above process.

*On the forces that circulate the blood.*

The due performance of the functions of circulation and respiration is as essential to the metamorphosis of the blood as it is to life itself.

Circulation commences in the fœtus with the rhythmic movements of the heart.

Reichert<sup>1</sup> has observed in the incubated egg, that the only independently formed canals for the blood are the great vascular trunks directly connected with the heart; the other blood-vessels are, as it were, excavated by the force of the heart's action on the blood-cells in the loose cellular mass of the early embryo.

The action of the heart is the *primum movens* of the circulation. Burdach<sup>2</sup> observes that the vital action of the heart, which acts mechanically on the blood, and propels it in certain directions and courses, indicates most clearly that the heart comprehends within itself the elements of the circulating power, and that independently of its vital activity, the whole circle of phenomena appertaining to it results from its mere mechanical relations. The cause of the heart's action must be referred to the irritation produced in it by the living blood. Müller<sup>3</sup> also considers that the blood is chiefly propelled by the rhythmic action of the heart.

The view taken by Schultz<sup>4</sup> is different: he considers that the motion of the blood in the living body results from the joint influence of the blood and of the vessels reciprocally acting on each other, whose true nature can only be seen in the vital relations, and its aim in the circle of organic functions.

R. Wagner<sup>5</sup> is inclined to believe that the blood is propelled

<sup>1</sup> Op. cit. p. 142.

<sup>2</sup> Op. cit. vol. 4, p. 163.

<sup>3</sup> Op. cit. vol. 1, p. 163.

<sup>4</sup> Op. cit. p. 244.

<sup>5</sup> Zur vergleichenden Physiologie des Blutes, 1833, p. 70.

not merely by the heart's action, but also by a certain electric attraction of the organs, by the influence of the nerves, and by a motive power inherent in the blood itself. Since the heart's action is occasioned by the irritation exercised upon that organ by the living blood, there can be no doubt that the reciprocating action of the organs and of the blood must influence the circulation. Schultz evidently undervalues the influence of the rhythmic motion on the circulation, when he limits the functions of the heart to the conveyance of arterial blood to the peripheral system, and to the conduction of venous blood back again, and regards the blood in the peripheral system as moving entirely independent of it.

The circulation is usually divided into the greater and the lesser. There is however, in fact, but one circulation; and this is divided into the greater course, which proceeds from the left heart through the arteries of the body, and through the veins to the right heart, and into the lesser course, which reconducts the blood through the lungs from the right to the left heart.

#### *On the process of respiration.*

Respiration takes place through lungs, gills, tracheæ, or the integument.

Oxygen is indispensable for the process, although pure oxygen is less conducive to health than a mixture of oxygen with a gas not detrimental to life, as nitrogen or hydrogen.

The proportions of oxygen and nitrogen that occur in atmospheric air are doubtless the most suitable for the respiration of the higher animals; viz. 21 parts of the former, and 79 of the latter gas. In an atmosphere of pure hydrogen or nitrogen, a man would run the risk of suffocation in a very few seconds, not because these gases are themselves poisonous, but simply from the absence of oxygen.

Many gases produce a directly poisonous effect, and cannot be breathed even when mixed with oxygen; as, for instance, arseniuretted hydrogen, sulphuretted hydrogen, phosphoretted hydrogen, carburetted hydrogen, carbonic oxide, cyanogen, chlorine, ammonia, and many others.

As a consequence of the process of respiration, the blood becomes chemically changed; this change is almost entirely confined to the blood-corpuscles, which in this independent

act of metamorphosis represent exactly what we understand by the vitality of the blood.

Respiration in man and the mammalia is effected by the dilatation and contraction of the cavity of the thorax.

Since the diaphragm in a state of relaxation is arched, and in a state of contraction during inspiration becomes flattened, the cavity of the thorax is increased during inspiration, the surface of the lung follows the retreating walls, its volume becomes enlarged, and the atmospheric air rushes into its cells. The branches of the air-tubes ramify to an extraordinary degree in the parenchyma, and their most minute extremities terminate in vesicular dilatations, which do not communicate with each other, and whose walls are covered with the peripheral capillary network. From a calculation of Lieberkuhn,<sup>1</sup> it would appear that the whole surface of the ramifying air-tubes in man amounts to 1400 square feet, on which extraordinary surface the blood and atmospheric air are in contact with each other, (being separated merely by a moist, permeable membrane,) and the former absorbs the required amount of oxygen.

Davy calculates that the human lung after the strongest expiration, still contains 35 cubic inches of air; after an ordinary expiration 108 cubic inches; after an ordinary inspiration 118, and after a very deep inspiration 240 cubic inches.

In ordinary inspiration and expiration (about 26 or 27 in the minute) the amount of air that is changed varies from 10 to 13 cubic inches.

According to Herbst, full-sized adults usually inspire from 20 to 25 cubic inches; persons of smaller stature from 15 to 20. The volume of air inspired during each respiratory act is fixed by Allen and Pepys at 16.5, by Abilgaard at from 3 to 6, and by Thomson at 40 cubic inches.

The quantity of air that enters the lungs in the course of 24 hours is calculated by Davy at from 400,000 to 500,000 cubic inches, by Allen and Pepys at from 460,800 to 475,200, and by Thomson at as much as 1,152,000, or 52.5 pounds, the respirations in this case being 20 in the minute.<sup>2</sup>

Atmospheric air once respired is lessened in volume; and

<sup>1</sup> Schultz, *op. cit.* p. 288.

<sup>2</sup> Gmelin's *Handbuch der theoretischen Chemie*, vol. 2, p. 1519.

the loss has been variously estimated by Berthollet, Pfaff, and Davy at from 1-27th to 1-100th of its bulk. Allen and Pepys, however, found the loss not more than 1-166th, or about 0.6%, and they looked upon the former as a mere error of observation.

The most important experiments regarding the changes which atmospheric air undergoes in respiration, are those of Allen and Pepys,<sup>1</sup> of Dulong,<sup>2</sup> and of Despretz.<sup>3</sup>

The earlier experiments of Allen and Pepys showed that the quantity of oxygen lost was exactly replaced by the carbonic acid generated, and that nitrogen was given off.

In their later experiments, it appeared that more oxygen was absorbed than the quantity of carbonic acid expired accounted for; they were also further convinced of the accuracy of their former observations respecting the increased quantity of nitrogen which is expired. They caused animals to breathe an atmosphere of pure oxygen, and likewise of oxygen mixed with three times its volume of hydrogen. In the latter case a portion of the hydrogen disappeared, and was replaced by an equal volume of nitrogen.

The experiments of Dulong were conducted with great accuracy, and by means of apparatus expressly prepared for the purpose. They showed that more oxygen is consumed than is replaced by the carbonic acid formed. The quantity of oxygen thus lost, and not replaced by carbonic acid, amounted in the case of herbivorous animals to about 10% of the oxygen which was changed into carbonic acid; in carnivorous animals the minimum excess amounted to 20, and the maximum to 50%.

The observations of Despretz confirm the results obtained by Dulong, and likewise show that nitrogen is developed during respiration.

The following table presents a sketch of the results of the observations made by Despretz; the calculations are founded on the French litre:—

<sup>1</sup> Schweiger's Journal, vol. 1, p. 182; and vol. 57, p. 337. Phil. Trans. 1809, p. 410.

<sup>2</sup> Ib. vol. 38, p. 505.

<sup>3</sup> Annales de Chimie et de Physique, vol. 26, p. 337.



	Air before the Experiment.		Air after the Experiment.			Excess of Oxygen over Carbonic Acid formed.	Nitrogen developed.
	Nitrogen.	Oxygen.	Nitrogen.	Oxygen.	Carbonic Acid.		
Rabbits . .	37·914	10·079	38·743	6·023	3·076	0·980	0·839
Leverets . .	39·085	10·389	39·517	6·216	2·955	1·218	0·432
Guinea-pigs	37·957	10·089	39·023	6·790	2·588	0·707	1·066
Dog . .	37·649	10·008	39·022	4·424	3·768	1·806	1·374
Puppies . .	37·176	9·882	38·273	3·649	4·018	2·215	1·097
Tom Cat . .	37·830	10·055	38·354	7·125	2·060	0·870	0·524
Pigeons . .	37·662	10·012	38·372	6·826	2·451	0·735	0·710
Great Owl .	38·027	10·109	38·754	7·483	1·601	1·025	0·727

The quantity of carbonic acid formed in the process of respiration in twenty-four hours in adults, and the amount of carbon contained therein, have been calculated as follows :

	Expired Carbonic Acid		Carbon.	Consumed Oxygen.	
	Cubic in.	Grains.	Grains.	Cubic in.	Grains.
Lavoisier and Seguin . .	14930	8584	2820	46037	15661 French.
Menzies . . . .	. . .	. . .	. . .	51480	17625 English.
Davy . . . .	31680	17811	4853	45504	15751 "
Allen and Pepys . . .	39600	18612	5148	39600	13464 "

The large amount of carbon, from 11 to 13 ounces, (Davy, Allen, and Pepys,) that is thus carried off by the lungs in the twenty-four hours, does not accord with the other phenomena of nutrition ; and Berzelius has calculated that it would require  $6\frac{1}{4}$  pounds of solid food daily to make up for the carbon that is separated by the lungs alone, without taking into consideration the very considerable amount that is also removed by the urinary secretion. And further : when we consider that in most sorts of food the portion which is converted into chyle is much less than that which is carried off by the intestinal canal in the form of fæces, it becomes the more wonderful how so many persons can exist on a few pounds of daily food, the solid constituents of which must be very small, and of which only a still smaller part admits of assimilation ; and we cannot help agreeing with Berzelius, that so large an excretion of carbon is inconceivable, and that in all probability there is some fallacy in the experiments.

Prout has made some interesting observations respecting the development of carbonic acid from the lungs at different

periods of the day. He found that during equal spaces of time the minimum occurred during the middle of the night; towards morning it increased, and attained its maximum between 11 and 1 o'clock; it then gradually diminished till about 9 p.m., when it remained fixed at its minimum till 3 a.m. The quantity of carbonic acid was likewise found to increase by gentle exercise, especially at its commencement, and when the barometer was low.

The mean amount of carbonic acid per cent. was 3.45. [A series of similar experiments has been published by Mr. Coathupe, which differ in several respects in their results from those of Prout. They were continued for a week. The following is the result obtained:

	Carbonic acid per cent. of air expired.
From 8 a.m. to 9½ . . . .	4.37
10 a.m. to 12 . . . .	3.90
12 noon to 1 . . . .	3.92
2 p.m. to 5½ . . . .	4.17
7 p.m. to 8½ . . . .	3.63
9 p.m. to midnight . . . .	4.12—Mean 4.02.

Macgregor ascertained that the air expired by persons ill of confluent smallpox contained as much as 8% of carbonic acid. During the eruptive fever of measles, it amounted to from 4 to 5%; and in proportion as the health was restored, the per centage was diminished to its natural standard. In chronic skin diseases an augmentation was likewise observed; and, in a case of ichthyosis, the mean per centage was 7.2; in typhus, according to Dr. Malcolm,<sup>1</sup> the formation of carbonic acid is diminished; in diabetes, no deviation from the normal standard could be detected.

The question of the quantity of carbonic acid expired by a person in twenty-four hours has lately become of peculiar interest, in consequence of its association with several problems of high physiological importance. Liebig has endeavoured indirectly to estimate the quantity by comparing the amount of carbon contained in the food consumed in the twenty-four hours, with the carbon of the excretions during the same period, and estimating the difference as the quantity separated by the respiratory process. He thus found that an adult, taking moderate exercise, expires daily on an average 13.9 ounces of carbon (more than double the quantity found by Lavoisier.)

<sup>1</sup> London and Edinburgh Monthly Journal of Medical Science, 1843, page 1.

Experiments have recently been made by Andral and Gavarret, Scharling, and Brummer and Valentin, with the view of ascertaining this point, and of elucidating the chemical bearings of this department of physiology. We shall endeavour to give, as briefly as possible, their most important results.

*Absolute quantity of expired carbonic acid.*

Andral and Gavarret expressed their results per hour. They are contained in the following table :

MALE SEX.							
Age.	Muscular development.		Carbon exhaled per hour.	Age.	Muscular development.		Carbon exhaled per hour.
			grains				grains
8	Moderate	.	67.0	37	Moderate	.	164.7
10	Very great	.	104.7	40	Very great	.	186.3
12	Moderate	.	113.9	45	Very slight (mean of 4)	.	132.4
12	Great	.	127.8	48	Good	.	161.7
14	Moderate	.	126.2	50	Good	.	164.7
16½	Good	.	157.0	54	Very great	.	163.2
18	Good	.	169.4	59	Moderate	.	154.0
20	Good	.	166.3	60	Extraordinarily great	.	209.4
24	Moderate (mean of 2)	.	176.6	63	Extraordinarily great	.	190.9
26	Extraordinarily great	{	217.1	64	Slight	.	133.9
			217.1	68	Moderate	.	147.8
26	Moderate	.	169.4	76	Slight	.	92.4
28	Good	.	190.9	92	Extraordinarily great	.	135.5
32	Good	.	176.6	102	Extremely diminished	.	90.8
33	Moderate (mean of 6)	.	164.7				

FEMALE SEX.							
Periods of life.	Age.	Muscular development.	Carbon exhaled per hour.	Periods of life.	Age.	Muscular development.	Carbon exhaled per hour.
			grains				grains
Prior to the appearance of the catamenia.	10	Good	92.4	After cessation of catamenia.	38	Moderate	120.3
	11	Good	95.4		42	Good	127.8
	13	Great	97.0		44	Very great	152.4
	15½	Very great	109.3		49	Moderate	113.9
During menstrual life.	15½	Moderate	97.0	3 months pregnant.	52	Moderate	115.5
	19	Very great	107.8		56	Moderate	109.3
	22	Good	103.1		63	Moderate	106.2
	26	Slight	92.4		66	Moderate	104.7
	26	Moderate	97.0	5 mo. do.	76	Very great	101.4
	32	Moderate	95.4		82	Moderate	92.4
	45	Moderate	95.4		42	Good	120.3
				5 mo. do.	32	Good	126.7
				7½ mo. do.	18	Slight	112.4
				8½ mo. do.	22	Good	129.3

It is thus seen that, in general, the amount of carbonic acid expired by both sexes increases with age up to a certain point—the 40-45th year, and then diminishes; that the quantity of carbonic acid expired increases with the development of the muscular system; that women expire less carbonic acid than men; that the formation of carbonic acid attains its maximum at the commencement of menstruation, and then experiences no further increase, except in the pregnant state, until the cessation of menstruation, when an increase again takes place. On an average, an adult male, of moderate constitution, exhales from 160 to 170 grains of carbon per hour; an adult female in the unimpregnated state, from 100 to 110 grains; during pregnancy, 125 grains; and after the cessation of the catamenia, from 116 to 130 grains. Dumas also found 154 grains per hour as the average quantity of carbon exhaled by an adult male.

Scharling's experiments were made on the following individuals: 1st, a male, æt. thirty-five, weighing 131 lbs.; 2d, a male, æt. sixteen, weighing 115½ lbs.; 3d, a soldier, æt. twenty-eight, weighing 164 lbs.; 4th, a girl, æt. nineteen, weighing 111½ lbs.; 5th, a boy, æt. nine and three-quarters, weighing 44 lbs.; and 6th, a girl, æt. ten, weighing 46 lbs. The carbon exhaled per hour amounted to—

No. of the person.	Amount of carbon. grains.	Remarks.	No. of the person.	Amount of carbon. grains.	Remarks.
1.	145	Fasting	3.	137·8	Asleep
In June	190	{ After breakfast and a walk	In	111·9	Fasting
when	130		October.	159·4	{ Fasting, after breakfast and work
very	165	Hungry		188·9	
hot.	160	2 hours after dinner		194·7	After dinner
	160	After tea		178·3	3 hours after dinner
	100	Whilst asleep		122·3	After work
					Whilst asleep
2.	114	Sleepy	4.	98·9	Whilst eating
In June	144·2	Fasting	In	91·3	Fasting
when	139·8	Fasting and hungry	October.	92·6	After supper
very	177	{ ½ an hour after breakfast		133·8	1 hour after breakfast
hot.	167·7			117·0	1 hour after dinner
		{ 2½ hours after breakfast		108·9	Whilst eating
	180·8				
		2 hours after dinner			



No. of the person.	Amount of carbon. grains.	Remarks.	No. of the person.	Amount of carbon. grains.	Remarks.
5.	76.2	Fasting	6.	65.5	Whilst asleep
In	94.8	Whilst at breakfast	In	95.3	After breakfast
Autumn.	113.8	After breakfast	Autumn.	103.0	After dinner
	119.3	1 hour after dinner		99.0	Shortly after tea
	84.5	2 hours after supper		75.1	Whilst asleep
	74.8	Whilst sleepy			

Supposing that adults sleep seven and children nine hours per day, the amount of carbon consumed is on an average—

	In twenty-four hours.	In one hour.
1.	3380 grains.	141 grains.
2.	3455	144
3.	3692	154
4.	2555	106
5.	2050	86
6.	1932	80

It is thus evident that the quantity of carbonic acid expired is very variable, and that it may be altered by many circumstances. Hunger and rest diminish, satiety and labour increase it. It is greater during the day than the night, in the proportion of 1.237 to one. If the expired carbonic acid be estimated in relation to the weight of the body, it is found that children give off a proportionally greater amount of this gas than adults. In some forms of disease, the amount of expired carbonic acid falls below the standard; it seems, in a state of health, to vary directly with the activity of the circulation.

The influence of muscular activity on the amount of carbon consumed, has been clearly shown by some experiments made by Dr. Hofmann during a pedestrian tour. His diet was simple and scanty, he took no drink, walked during the whole day, weighed all his food and every excretion that could be weighed (even the nasal mucus), as well as himself; he then found that the weight lost by the body was never equalled by the excess of the excrements over the food, and that there was a constant loss of matter by the skin and lungs, which amounted to more than 1 lb. We must pass over the details of his experiments. Brunner and Valentin found that the weight of carbon they consumed per hour varied from 134 to 170 grains, and averaged 160. The volume of expired carbonic acid per hour, on an

average, was equal to 21·8 litres,<sup>1</sup> and the entire volume of the air expired per hour on an average equal to 5·40 litres. These results agree well with those of the earlier observers. When the corrections for moisture are made, the quantity of carbon expired per hour is equal on an average to 172 grains, and of carbonic acid 23·5 litres.

*B. Relations of the constituents of the expired air to the theory of respiration.*

On this point Brunner and Valentin only have experimented. They found—

Individual.	No. of experiments.	Volume per cent.			Volume per cent. in relation to the atmosphere.		
		Mean of	CO <sub>2</sub> .	O.	N.	Disappeared O.	Difference of N.
Brunner	12 exp. 1st series		4·356	16·907	79·547	4·720	+ 0·362
	4 exp. 2d „		3·825	16·306	79·869	4·508	+ 0·683
Thomas	4 exp. 1st „		4·673	15·895	79·432	4·920	+ 0·329
Valentin	2 exp. 1st „		4·316	16·143	79·541	4·671	+ 0·356
	12 exp. 2d „		4·641	15·783	79·576	5·032	+ 0·391
Total average			4·380	16·033	79·587	4·783	+ 0·402
Weight per cent.							
Brunner	12 exp. 1st series		6·522	17·428	76·050	5·582	— 0·940
	4 exp. 2d „		5·749	17·735	76·516	5·275	— 0·474
Thomas	4 exp. 1st „		6·975	17·165	75·860	5·845	— 1·130
Valentin	2 exp. 1st „		6·458	17·481	76·061	5·529	— 0·929
	12 exp. 2d „		6·945	17·089	75·965	5·920	— 1·025
Total average			6·546	17·373	76·081	5·637	— 0·909

It is thus evident that the variations observed in the amount of nitrogen are entirely within the errors of observation, and the nitrogen may be disregarded in the process.

Again, the expired air contains a volume of carbonic acid, which is but little less than the volume of oxygen which has disappeared (therefore the weight per cent. of the carbonic acid is necessarily somewhat greater than that of the absorbed oxygen, and thus also the difference of nitrogen appears positive as regards volume, but negative as regards weight); so that all the oxygen absorbed reappears as carbonic acid, except a small quantity consumed in the body for other purposes. Now, according to Graham's law of the diffusion of gases, when they are separated by an animal membrane and are under equal pressure, they become mixed inversely as the square roots of

[<sup>1</sup> The litre is a little larger than the English wine quart; the litre being equal to 1·028, and the quart to 57·75 cubic inches.]

their densities; consequently, 1·17585 volume of oxygen is absorbed for one volume of expired carbonic acid. Comparison of the figures shows us that the mixture of the two gases in respiration takes place entirely according to the law of diffusion of gases; for the most accurate method of experimenting gave results, in which the figures obtained for the carbonic acid and absorbed oxygen, almost exactly agreed with those reckoned according to the law of the diffusion of gases :

Volume per cent. of the expired air.			Oxygen absorbed.	Carbonic acid calculated.	Difference.	
CO <sub>2</sub> .	O.	N.				
3·850	16·270	79·185	4·690	3·994	+	0·144 per cent.
3·593	16·034	79·185	4·931	4·199	+	0·606 „
3·949	16·090	79·185	4·887	4·162	+	0·213 „
3·777	16·090	79·185	4·914	4·192	+	0·415 „
3·759	16·095	79·185	4·922	4·192	+	0·433 „
4·483	15·328	79·185	5·698	4·853	+	0·370 „
4·752	14·733	79·185	6·362	5·418	+	0·660 „
4·588	14·852	79·185	6·253	5·325	+	0·737 „

In respiration, which is thus a purely mechanical process, the inspired air is first warmed to 99°·5, and saturated with moisture at this temperature, which is rapidly accomplished on account of its extensive distribution. It then experiences a simple diffusion; the nitrogen remains entirely unaffected; 1·1742 volume of oxygen is absorbed, and replaced by 1 volume of carbonic acid which is expired; or for each volume of oxygen absorbed ·8516 volume of carbonic acid appears. In consequence of the accuracy with which the law of diffusion is here observed, the most minute portion only of other gases is absorbed or expired.

That hydrogen, carburetted hydrogen, and carbonic oxide gases are not contained in the expired air, the authors have shown by some direct experiments; but small quantities of organic matters are evolved during respiration, as is shown by sulphuric acid, through which expired air has been made to pass, being always coloured red.]<sup>1</sup>

Various opinions have been promulgated respecting the formation of carbonic acid in the blood. The most natural and probable is that of Lagrange and Hassenfratz, who maintain that the blood takes up oxygen in the lungs and retains it in a

<sup>1</sup> [For further information on this subject, the reader is referred to Valentin's *Lehrbuch der Physiologie*, 1844, vol. 1, pp. 507–580, or to an excellent abstract that appeared in the *Chemical Gazette*.]

state of solution. The blood-corpuscles absorb from this constant source a due supply of oxygen for their change.

The metamorphosis occurs in the peripheral system, and, for the most part, in certain organs, as, for instance, the kidneys. The blood-corpuscles give up the carbonic acid, thus formed, to the blood, and it is thrown off by the lungs. It must be remembered that blood always contains carbonic acid and oxygen, but arterial contains more of the latter and less of the former than venous blood; also, that the whole of the carbonic acid is not separated by the lungs, although, when the blood reaches those organs, it is perfectly free from oxygen.

Although the atmospheric air and the circulating fluid are not brought into absolute contact, there is no impediment to their mutual action. The absorption of the air through the humid membrane that surrounds the parenchyma of the lungs is facilitated by the immense extent of surface presented, over the whole of which a thin stratum of blood is distributed, and simultaneously exposed to the atmospheric influence. The permeability of the soft tissues, especially of the membranes, by fluid and gaseous substances, is a well known fact. It is in accordance with this law that atmospheric air finds its way into the blood. Dark red blood, inclosed in a moist bladder, soon assumes a bright red tint; a gas inclosed in a similar receptacle is found, after some time, to be partly displaced by atmospheric air. These are mere illustrations of the same principle. If the opinion that has just been given be correct, then carbonic acid and oxygen must be present both in venous and arterial blood. Numerous experiments have been instituted with the view to determine this point.

By submitting 12 ounces of the venous blood of a calf to a heat of 200°, Sir H. Davy obtained 1·1 cubic inch of carbonic acid, and 0·7 of oxygen, and the experiment has been confirmed by Brande and Vogel. Stromeyer, Bergemann, Müller, and others have failed in obtaining carbonic acid from blood in this manner. Brande and Vogel found that blood placed *in vacuo* developed a gas which contained some carbonic acid, and their statement is confirmed by Home, Bauer, and Reid Clanny, while J. Davy,<sup>1</sup> Mitscherlich, Tiedemann, Gmelin, and Müller

<sup>1</sup> [Dr. Davy has recently shown that gas is frequently, although not invariably, disengaged both from venous and arterial blood *in vacuo*. Researches, Physiol. and Anat. vol. 2, p. 153.]



failed in observing any development of carbonic acid under the air-pump.

Hoffmann and Stevens could not obtain carbonic acid either by the application of heat or by the air-pump; but they observed that if freshly-drawn blood be shaken with hydrogen, carbonic acid is then evolved. Another experiment in favour of the existence of carbonic acid in the blood has been instituted by Müller. Nysten and Collard de Martigny made animals inhale gases entirely devoid of oxygen, and observed the formation of carbonic acid. Müller and Bergemann made frogs breathe pure hydrogen and nitrogen, and observed that, after the animals had remained in these gases from 6 to 22 hours, they had expired a quantity of carbonic acid, varying from 0.25 to 0.83 of a cubic inch.

Magnus has published a series of accurate experiments which must be regarded as quite decisive respecting the amount of carbonic acid and oxygen in arterial and venous blood. He passed a current of hydrogen through recently drawn blood, and found that carbonic acid was given off in a constantly decreasing ratio. He likewise analysed the whole of the gas that he obtained from the blood, and found its composition as follows :

Volumes in cubic centimeters.					Gas.	
Blood of a horse	.	.	.	125	.	yielded 9.8 { 5.4 CO <sub>2</sub> 1.9 O 2.5 N
Venous blood of a horse	.	.	.	205	.	12.2 { 8.8 CO <sub>2</sub> 2.3 O 1.1 N
Ditto	.	.	.	195	.	14.2 { 10.0 CO <sub>2</sub> 2.5 O 1.7 N
Arterial blood of a horse	.	.	.	130	.	16.3 { 10.7 CO <sub>2</sub> 4.1 O 1.5 N
Ditto	.	.	.	122	.	10.2 { 7.0 CO <sub>2</sub> 2.2 O 1.0 N
Venous blood of the same horse	.	.	.	170	.	18.9 { 12.4 CO <sub>2</sub> 2.5 O 4.0 N
Arterial blood of the calf	.	.	.	123	.	14.5 { 9.4 CO <sub>2</sub> 3.5 O 1.6 N

Volumes in cubic centimeters.				Gas.	
Arterial blood of the calf	.	.	108	.	yielded 12.6
					{ 7.0 CO <sub>2</sub>
					{ 3.0 O
					{ 2.6 N
Venous blood of the same calf	.	.	153	.	13.3
					{ 10.2 CO <sub>2</sub>
					{ 1.8 O
					{ 1.3 N
Ditto	.	.	140	.	7.7
					{ 6.1 CO <sub>2</sub>
					{ 1.0 O
					{ 0.6 N

From these experiments, it follows, 1st, that carbonic acid, oxygen, and nitrogen exist both in arterial and in venous blood; and, 2dly, that the quantity of oxygen is greater, and the quantity of carbonic acid less in arterial than in venous blood, a fact which confirms the opinion we have expressed regarding the formation of carbonic acid and the theory of respiration generally.

The bright colour which is communicated to the blood by oxygen, as well as the dark shade that is induced by the transmission of carbonic acid through it, are the actual shades of colour that we see in arterial and venous blood. Moreover, when blood has been rendered artificially venous in this way, it may be rendered arterial in its colour by agitation with a certain quantity of oxygen, and we can then obtain from it a mixture of oxygen and carbonic acid.

We have now enumerated the most interesting phenomena in reference to the expired air. We have already noticed the circumstance that nitrogen is expired. It follows naturally that this gas, which forms the principal constituent of the atmosphere, should be inhaled; and, according to Edwards, there is a sort of compensation between the amount of exhaled and inspired nitrogen, so that the quantity of this gas in the atmosphere remains fixed, the amount of expired nitrogen predominating at one time, and of inspired nitrogen at another. According to Berzelius, the portion of nitrogen taken up by the blood is only changed when the blood comes in contact with a gas which either contains no nitrogen or which possesses it in a greater ratio than atmospheric air. Nitrogen is therefore evolved from the blood during the inspiration of oxygen or hydrogen, and the circulating fluid is then found to contain a greater proportion than usual of oxygen or hydrogen; but if nitrogen is inhaled, an excess of this gas is found in the blood, while oxygen and carbonic acid are evolved in accordance with the known law of the diffusion of gases.

In the air after expiration we always find a greater or less amount of watery vapour. According to Menzies, an adult man, in the course of twenty-four hours, gets rid, in this manner, of 2880 grains of water. Abernethy fixes the amount at 4320; Thomson at 9120; Hales at 9792; and Lavoisier at as much as 13,704 grains. This water exhales from the blood which is circulating in the bronchi and cavity of the throat, and contains some animal matter which causes it to decompose speedily. Alcohol, ether, and substances of that nature are removed from the blood by the lungs, at least in part; for after they have been taken, their odour may be distinctly recognized in the breath. Sulphuretted and phosphoretted hydrogen, if injected into a vein, are easily recognized in the breath by the odour; and if phosphoretted oil is applied in a similar manner, dense white vapours of phosphorous acid are speedily exhaled.

*Respiration of the fœtus and of animals.*

As the function of respiration in the embryo of the mammalia cannot be carried on by the lungs, an equivalent is supplied to them by the influence of the maternal fluids on those of the fœtus, in the placenta. Anatomical investigations have shown, that it is impossible for the blood of the mother to be transmitted unchanged into the fœtus; nutriment and arterial blood can only make their way into the fœtal system through the medium of cells.

In the umbilical cord there are two vessels which convey venous blood from the fœtus to the placenta, and there is one that conducts arterial blood from the placenta to the fœtus. The changes which are effected in this manner in the fœtal blood are not so obvious as if they had occurred in the ordinary manner in the lungs: in fact it is by no means easy, or indeed always practicable, to detect any difference in the colour of the arterial and venous fœtal blood. The change, however, such as it is, is of the highest importance to the fœtus, since it dies if the umbilical cord be tied before birth. The anatomical peculiarities in the circulating system of the fœtus are too well known to require any description.

In the embryo of birds the respiration is carried on during the later stages of development, by the allantois, an extremely vascular membrane, over which the left umbilical artery is

especially distributed. The embryo is ultimately entirely inclosed in the *allantoide* (the *chorion* of V. Baer,) and is intimately connected with the membrane of the shell. The mutual action of the allantoide and the atmosphere, takes place directly through the membrane of the shell, and the shell itself, and thus it may be regarded as a proper respiratory organ, whose development has corresponded throughout with that of the embryo.

In birds, the lungs do not occupy the whole of the thoracic cavity, but are placed in its furthest extremity: the thoracic and abdominal cavities are not separated by a diaphragm. Openings are situated on the surface of the lungs which admit the air from those organs into the large cells situated around the pericardium and between the viscera of the abdomen: the air can pass from these cells even into the cavities of the bones.

Respiration is conducted in fishes much on the same principle that it is in the fœtus of the mammalia. The venous blood is conveyed to the gills, where it circulates in the capillaries, and absorbs oxygen and nitrogen from the air which is contained in the water, and in this way it becomes arterialized. Humboldt and Provençal have carefully studied the process of respiration in fishes, and have proved that they take up oxygen and nitrogen from the air which is diffused through the water, and that they exhale carbonic acid; that the quantity of oxygen which they absorb is more than is replaced by the carbonic acid expired; that fishes absorb oxygen from boiled water which has been subsequently impregnated with half its volume, but that they only survive in it for a short time; and, lastly, that they die in water from which the air has been removed, or in which they have respired for any time.

The water (from the Seine) in which these experiments were conducted contained from  $\cdot 0266$  to  $\cdot 0287$  of its volume of atmospheric air, of which from  $\cdot 306$  to  $\cdot 314$  was oxygen. The amount of carbonic acid varied from  $\cdot 06$  to  $\cdot 11$  of the volume of atmospheric air.

The water was inclosed in bell-glasses over mercury, through which the fishes were introduced into it. In experiments with tenches they observed, that from 100 parts of atmospheric air there were abstracted 22·8, 13·6, 23·4, 15·5, 17·4, 22·8 parts, the variations depending on the duration of the experiment



and the number of the fishes. The ratios of the consumed oxygen to the carbonic acid formed, were as 1 to .57, .80, .91, .20, and .50, while the ratios of the consumed oxygen to the consumed nitrogen were as 1 to .43, .87, .40, .19, .71, and .63. The inequality of these ratios indicates, as Berzelius remarks, the varying power with which fishes act upon the air on different days, at different seasons, and possibly in different conditions of health.<sup>1</sup>

The amount of oxygen consumed by fishes is much less than would be required for warm-blood animals of equal bulk,<sup>2</sup> and their temperature is very little above that of the surrounding medium. When breathing free atmospheric air, they do not consume more oxygen than in their native element.

Fishes absorb oxygen and exhale carbonic acid, not merely with their gills but with the whole surface of their body, as long as they are surrounded with water impregnated with atmospheric air. This fact was proved by Humboldt in the following manner. He passed a cork collar, covered with waxed cloth, over the head of a fish, which was then introduced into a vessel filled with water, the vessel being closed by the cork collar, which was so adjusted that the head and gills of the fish did not come in contact with the water in the vessel. Fishes thus treated lived five hours, and the water in the vessel underwent the changes usually produced by respiration.

Ermann found that the air, in the swimming bladder of lake fish, is deprived of a considerable portion of its oxygen. Biot, on the contrary, found in the swimming bladder of those marine fishes that inhabit deep waters, more oxygen than nitrogen. Humboldt and Provençal observed that after the removal of the swimming bladder fishes continued to absorb oxygen, but that they did not form any carbonic acid; they regard it, however, as doubtful whether this phenomenon is due to the pathological condition of the animal, or to the absence of the swimming-bladder.

Insects can live for a long time under the receiver of the air-pump, in a very rarified atmosphere; if, however, their stig-

<sup>1</sup> *Thierchemie*, p. 140.

<sup>2</sup> Treviranus estimates the amount at about 50% less than warm-blood animals of equal bulk would consume. His conclusions are based on the experiments referred to in the text.

mata be closed with oil, they speedily die. The researches of Scheele, Vauquelin, and Hausmann show that in the respiration of insects a portion of the oxygen of the atmospheric air is converted into carbonic acid.

Treviranus has observed that the amount of oxygen which is taken up is frequently twice as great as is required for the production of the carbonic acid formed, and that insects always develop nitrogen. Thus a honey-bee, confined in an atmosphere of 272 cubic inches, consumed 13·5 of oxygen, while it only yielded 8·3 of carbonic acid and 5·3 of nitrogen.

The experiments of Spallanzani and Hausmann tend to prove that the changes produced by worms on the atmospheric air in which they are confined are similar to those effected by insects.

#### *On the metamorphosis of the blood.*

All our conceptions of organic life are associated with the idea of continuous change of substance. A constant metamorphosis is going on in the living blood, which, in fact, may be regarded as the most obvious manifestation of its vitality.

When it ceases to undergo this metamorphosis, it dies ; indeed the very act of vital annihilation is attended with a change in the blood, which we regard as an indication of its plastic power. As, however, life in every manifestation of its varying forms is dependent on certain conditions, and cannot exist when they are infringed, so it is with the vitality of the blood ; for although there is doubtless an actual inherent power in the blood, it can no longer act when it is deprived of the condition requisite for its maintenance, namely, the reciprocal action of the organism. The blood is not the only portion of the body that undergoes this change ; every organ and tissue is subjected to a similar metamorphosis, which is presented to us under the general phenomena of nutrition and consumption, (or waste,) and which is dependent on, and effected by, the blood alone ; but since the various tissues present a different chemical composition, and since the different organs separate different matters from the blood, it is obvious that they cannot all modify the circulating fluid in the same manner, but that the metamorphosis must vary in some degree with the influence of the nervous system. Two conditions are essentially requisite for the metamorphosis of the blood, namely, circulation

and respiration, inasmuch as, without them, the blood would not be brought in contact with the oxygen, which is necessary for the existence of life; and the more completely these functions are discharged, the more perfectly will the due changes in the blood be effected; if, on the contrary, the blood is detained in any part of the body, or cannot enter the sphere of atmospheric action in the lungs, the metamorphosis can be only imperfectly effected.

We know, from the investigations of Schwann and Reichert, that all the tissues of the animal body are composed of cells, and that nutrition and growth of the organs and tissues is conducted by the production of new cells, appropriate for each individual organ, developing themselves at every point where the substance from which they are formed, viz. the blood, is conveyed; that these cells, by their organic formation, effect a change in the nutritious plasma, by appropriating from it matters homologous to themselves, and that the cells are finally consumed or dissolved, as is obvious from the general phenomena of the circulation. The nutrition and consumption of the tissues of the animal body in the general process of life is, consequently, the product of the nutrition and consumption of the cells which constitute those tissues. Since the capillaries are distributed over every particle of each individual tissue, and since their walls are composed of cells, which can communicate and impart the plasma to the adjacent cells, the plasma can be universally distributed, and the reciprocal action between it and the cells of the various organs ensured.

In what manner the cells act upon the nutrient fluid we are not able to understand, but there can be little doubt that they, or (which amounts to the same thing) the organs and tissues which they constitute, produce a dialytic, catalytic, or, as Schwann terms it, a metabolic change on the plasma of the blood. The products of these influences must necessarily consist of certain chemical compounds, formed in very different ways, and varying in their nature in accordance with the activity of the nervous power. The high atomic numbers of those animal substances which are of the most importance in nutrition, as the protein-compounds and fats, render the existence of numerous decompositions extremely probable. In vegetable chemistry we find whole classes of substances transmutable, one into the other, in which the

same radical, consisting of carbon and hydrogen, is combined with different atoms of water, or of water and oxygen; I need only refer to woody fibre,<sup>1</sup> starch, gum, sugar, and lactic acid. We have sufficient grounds for assuming the existence of similar radicals in the chemical compounds of the animal body; and if we knew more of the composition of the extractive matters, we should doubtless find a radical common to all of them. In many of these decompositions, which are extremely varying in their nature, oxygen is undoubtedly absorbed, and carbonic acid evolved, as indeed we see in the process of respiration. Oxygen combines not merely with carbon; it may also enter into combination with hydrogen and form water, or with a binary or ternary radical, which it would oxidize. Hydrogen and oxygen may, further, be either separated from or taken up by these compounds, in the proportions in which they form water. Thus quaternary compounds may be split into several quaternaries with the same or a different radical, or into quaternary and ternary compounds, &c. These must, however, be regarded as mere possibilities, which, unless kept in check by experiment, are capable of indeterminate extension.

One of the most important conditions for the reciprocal action between the cells of organs and the nutrient fluid is a proper degree of warmth; the requisite temperature varies in different classes of animals, but its range is limited within very narrow bounds, above or below which the action is impeded, or even destroyed, and death then ensues. If, therefore, we should regard the conditions of temperature as independent of the organism, and unconnected with the phenomena of life, these phenomena would be unavoidably and perpetually disturbed, and the due course of the organism altogether destroyed.

The conditions for the production of a due temperature are therefore based on the vital phenomena themselves, and in accordance with the principles of adaptation that are observed

<sup>1</sup> [Woody fibre (lignine)	•	$C_{12} H_8 O_8$	$= (C_{12} H_8) O_8$
Starch . . . .	•	$C_{12} H_{10} O_{10}$	$= (C_{12} H_8) O_8 + 2HO$
Gum . . . . .	•	$C_{12} H_{11} O_{11}$	$= (C_{12} H_8) O_8 + 3HO$
Cane sugar . . .	•	$C_{12} H_{10} O_{10} + HO$	$= (C_{12} H_8) O_8 + 3HO$
Grape or diabetic sugar	•	$C_{12} H_{11} O_{11} + 3HO$	$= (C_{12} H_8) O_8 + 6HO$
2 eq. Lactic acid .	•	$C_{12} H_{10} O_{10} + 2HO$	$= (C_{12} H_8) O_8 + 4HO.]$



in the animal organism, it is developed by those very processes for which its existence is indispensably necessary.

*On animal heat.*

The temperature of every animal is higher than that of the surrounding medium. The temperature of the human body in those internal parts which are most easily accessible, such as the mouth and rectum, is usually between  $97^{\circ}\cdot7$  and  $98^{\circ}\cdot6$ . The temperature of human blood varies from  $100^{\circ}\cdot6$  to  $101^{\circ}\cdot75$  in a state of health, but in disease it may rise to  $106^{\circ}$  or  $107^{\circ}$ . In morbus cœruleus and in cholera the temperature falls considerably: in the former the hand could only raise the thermometer to  $78^{\circ}\cdot8$ , and in the latter, the heat of the mouth raised it only to  $78^{\circ}\cdot8$ , and in another experiment to  $77^{\circ}$ . In healthy persons the temperature is said to attain its maximum during the day, and to fall from  $1\cdot8$  to  $2\cdot7$  degrees during sleep. In warm climates Dr. Davy found the temperature of the interior of the body  $2^{\circ}\cdot7$ - $3^{\circ}\cdot6$  higher than in temperate climates.

Tiedemann<sup>1</sup> has given the following table regarding the temperature of birds, which is higher than that of any other class of animals.

	Degrees.
Great titmouse . . . . .	111·25
Swallow . . . . .	111·25
Fringilla, different species . . . . .	111·25 to 107
Anas, different species . . . . .	111 to 106
Common hen . . . . .	109·94 to 102·99
Falco, different species . . . . .	109·74 to 104·5
Pigeon . . . . .	109·58 to 106·7
Raven . . . . .	109·23 to 105·99
Vulture . . . . .	107·49
Common cock . . . . .	103·78 to 102·99
White game . . . . .	102
Gull . . . . .	100

Tiedemann and Rudolphi have also made an extensive series of observations regarding the temperature of the mammalia. The following is derived from their tables :

	Degrees.
Bat ( <i>Vespertilio pipistrellus</i> ) . . . . .	106 to 105
Squirrel . . . . .	105
Sheep . . . . .	104 to 100·4

<sup>1</sup> Tiedemann's Physiologie, vol. I, p. 454.

	Degrees.
Ox . . . . .	104 to 99
Rabbit . . . . .	104 to 99·46
Ape ( <i>Simia aigula</i> ) . . . . .	103·86
Cat . . . . .	103·6 to 98·6
Bat ( <i>Vespertilio noctula</i> ) . . . . .	102
Dog . . . . .	101·3 to 99·3
Guinea-pig . . . . .	100·4 to 96·37
Hare . . . . .	100
Elephant . . . . .	99·25
Horse . . . . .	98·24 to 97

There is no very great difference between the cetacea and the other mammalia in respect to their temperature. The temperature of the seal and of the Greenland whale has been determined at  $104^{\circ}$ , and that of the porpoise has been found to vary from  $99^{\circ}\cdot 5$  to  $95^{\circ}\cdot 9$ . The temperature of the amphibia differs very slightly from that of the surrounding medium. Czermack<sup>1</sup> found that the temperature of a proteus was  $63^{\circ}\cdot 5$  when that of the air was  $55^{\circ}\cdot 4$ , was  $68^{\circ}\cdot 25$  when the temperature of the air was  $63^{\circ}\cdot 5$ , and was  $65^{\circ}$  in water at  $55^{\circ}$ ; in water of which the temperature was  $44^{\circ}\cdot 4$ , the temperature of a frog was  $48^{\circ}$ . Dr. Davy found the temperature of a snake  $88^{\circ}\cdot 46$  in air of  $81^{\circ}\cdot 5$ , and  $90^{\circ}$  in air of  $82^{\circ}\cdot 94$ ; the temperature of testudo midas was  $84^{\circ}$ , while that of the air was  $79^{\circ}\cdot 5$ .

The temperature of fishes appears, from the experiments of John Hunter, Dr. Davy, Broussinet, and others, to be from  $\cdot 7$  to  $2\cdot 7$  degrees above that of the surrounding water.<sup>2</sup>

It must be regarded as an established fact, that a certain temperature is necessary for the continuance of animal life, and that the source of this temperature must be sought for within the organism, and must be looked upon as a consequence of life itself. The production of heat cannot, however, be so properly ascribed to any of the collective phenomena of life, as to the chemical processes, which are known to develop warmth, and the action of which we see in the metamorphoses; and on

<sup>1</sup> Baumgärtner's und Ettinghausen's Zeitschrift für Physik und Mathematik, vol. 3, p. 385.

<sup>2</sup> [The theory of respiration, as the source of animal heat, invented by Lavoisier and Laplace, as well as the critical experiments by which that theory was tested by Dulong and Despretz, are too well known to require repetition; neither need we devote any space to the influence of the nerves on the generation of heat. The subject is fully discussed in Müller's Physiology, translated by Dr. Baly, vol. 1, pp. 83-88; first edition.]

the other hand a certain degree of animal heat is indispensably requisite for those chemical processes which are the necessary consequences of the proper organic development of the cells of all tissues, and of their catalytic influence on the nutrient fluid, the plasma of the blood. The animal heat is therefore to be regarded as the product of those vital functions, for the due exercise of which it is essentially requisite. The organism is thus protected against the innumerable disturbing forces under which it would otherwise succumb, in consequence of the varying temperature of the external world. The development of heat, therefore, decreases with the diminution of the vital powers, with the retarded circulation of the blood, with checked nutrition, and with imperfect metamorphosis, while all the phenomena of inanition, perfect destruction of power, and finally an asphyxiated condition, are the consequences.

As this cellular action, which is collectively exhibited in the metamorphosis of the animal organism, may be regarded as purely chemical, so the heat that is engendered thereby may be considered as a consequence of these chemical processes, and therefore all those functions of the organism which are necessary for the preservation of life, contribute directly or indirectly to the production of animal heat, which must be regarded as developed at every point at which metamorphosis is occurring, and therefore not merely in the lungs, but in the whole peripheral system. The absorption of oxygen, and its combination with the carbon of animal matter, not only in the lungs, but in the whole body, must, on that account, be regarded as the principal source of heat. In addition to the oxygen required for the formation of the carbonic acid, a certain amount is absorbed, which probably enters into combination with hydrogen, or with binary or ternary radicals of carbon and hydrogen, of carbon and nitrogen, or of carbon, hydrogen, and nitrogen, and in this manner, doubtless, contributes somewhat to the general production of heat.

The theory of animal heat affords a simple explanation of many well-known phenomena, as, for instance, of the slight independent warmth of the fœtus, when removed from the uterus (as shown by Autenrieth and Schultz),<sup>1</sup> and of those young

<sup>1</sup> *Experimenta circa calorem fœtus et sanguinem.* Tab. 1799.

animals that are born in an imperfectly developed condition.

The low temperature of persons with morbus cœruleus, in whom the metamorphosis of the blood is always imperfect, and the corresponding phenomena that are presented by aged, debilitated, sick persons, and those in whom (according to Edwards) a small quantity of blood circulates torpidly; as well as the increased temperature in inflammatory diseases when the blood circulates more rapidly than usual, and the metamorphosis is more rapid, are other illustrations of the same principle.

The phenomena observed in hibernating animals are strongly corroborative of the mutual dependence of the animal heat and of metamorphosis, and also of the intimate connexion of the former with the processes of respiration and circulation.

The observations of Pallas, Spallanzani, Mangili, Saissy, Czermack, and Berthold show that hibernation is prevented by a temperature of from  $50^{\circ}$  to  $80^{\circ}$ , whilst it is induced in those animals that are subject to it, even in summer, by means of artificial cold: other observers, however, maintain, that there is a periodical deficiency of vital energy at the usual hibernating season. During this peculiar state the respiration becomes slow, and may even cease altogether; the circulation is likewise almost stopped, for Saissy found that the capillaries of the external parts of the body were nearly empty, while the larger vessels were only half filled, and the undulatory motion of the blood was observable only in the principal trunks of the thorax and abdomen. He likewise found that the blood did not contain the usual amount of fibrin and albumen at this period, and that the bile had a peculiarly sweet taste.

The production of heat is also dependent on the mass of the blood-corpuscles, and on the rapidity of the circulation,—a view that perfectly accords with the preceding statement, for the corpuscles are (as we shall presently show) undergoing a constant metamorphosis, which may be regarded as an evidence of the vitality of the blood, and which is intimately connected with the respiratory process.

When there is a paucity of corpuscles, the necessity for the absorption of oxygen is diminished in a corresponding ratio, the circulation becomes slower, and there is less heat developed than in the normal state: on the other hand, blood with an



excess of corpuscles, but which is circulated slowly, develops less heat than blood which contains a smaller proportion of corpuscles, but which is more rapidly circulated, for more oxygen may be consumed in the latter than in the former case.

The following table, drawn up from the researches of Dumas and Prevost, and amplified by my own observations, affords some interesting data on this point:

Animal.	Blood-corpuscles.	Mean temperature.	Pulse.	Respiration.
Pigeon . . . .	15·57	107·6	136	34
Common hen . . . .	15·71	106·7	140	30
Duck . . . .	15·01	108·5	110	21
Raven . . . .	14·66	108·5	110	21
Heron . . . .	13·26	111·2	200	22
Ape ( <i>Simia Callitriche</i> ) .	14·61	95·9	90	30
Man . . . .	12·92	98·6	72	18
Guinea-pig . . . .	12·80	100·4	140	36
Dog . . . .	12·38	99·4	90	28
Cat . . . .	12·04	101·3	100	24
Goat . . . .	10·20	102·5	84	24
Hare . . . .	9·38	100·4	120	36
Horse . . . .	9·20	98·2	56	16
Sheep . . . .	9·20	100·4		
Ox . . . .	10·50	99·5	38	
Carp . . . .	2·10	51·1 to 51·4	20	
Tench . . . .	1·40	52·8 to 51·4		
Green toad . . . .	2·20	51·8 to 51·4	77	

The metamorphosis of the blood, and the general change of matter, lead to still another secondary source of animal heat. It has been shown by Pouillet<sup>1</sup> that all solid bodies, organic and inorganic, undergo an elevation of temperature when moistened with different fluids. In organic substances it may amount to from 11° to 18°. Since the act of metamorphosis is always effected through humid membranes, this source of heat must be regarded as of great importance, even if it be not actually identical with the catalytic metamorphosis of the cells themselves.

Becquerel and Breschet<sup>2</sup> have observed, by means of a thermo-electric multiplier, that each contraction of a muscle is accompanied by an increase of temperature, amounting to

<sup>1</sup> *Annales de Chimie et de Physique*, vol. 20, p. 141.

<sup>2</sup> *Annal. des Scienc. Nat.* 1835.

from  $1^{\circ}8$  to  $2^{\circ}6$ , the increased temperature that succeeds violent exercise may probably be in part accounted for by this means.

*Metamorphosis of the blood in the nutrition of the organism.*

The conveyance of nutriment to the various parts of the organism is one of the most important functions of the blood; and in order to discharge it efficiently, the blood must itself receive a constant supply of proper material.

Regarding the blood physically, as composed of corpuscles and plasma, it is only from the latter that the organs can directly obtain nourishment. This plasma is, however, a very complicated fluid; its principal constituents are albumen, fibrin, fatty compounds, salts, extractive matters, and a peculiar colouring matter, hæmaphæin. The question now arises, Are all these constituents, or only some of them, employed in nutrition? Our analyses of urine, sweat, and mucus show that these secretions and excretions carry off, in addition to certain peculiar matters, the same pigment, the same salts, and the same (or similar) extractive matters as are contained in the plasma; hence we may infer that those substances which are removed from the body are effete products of the metamorphosis, and that they are not suited for nutriment, at any rate in the form in which they occur. Neither albumen, fibrin, nor fat<sup>1</sup> is found in urine, sweat, or mucus, and the presence of either albumen or fat is always regarded as a symptom of a morbid state. This fact tends to support the opinion that albumen, fibrin, and fat are the substances which are employed in the nutrition of the peripheral system.

The blood, in its passage through the capillary network, permeates all organs and tissues, and their cells take up from the plasma those substances which they require for nutrition, and restore to it those which have become effete, and are no longer adapted for the process of nutrition. We may con-

<sup>1</sup> The fat that is occasionally to be detected in the sweat does not arise from the true perspiration, but from the sebaceous glands of the skin. Perfectly normal mucus, such as occurs in some quantity in healthy urine, contains neither albumen nor fat. Pulmonary mucus and the saliva discharged with it often contain a little fat and albumen, but, in all probability, they belong to the saliva only, a fluid not intended to be excreted.

clude that the act of nutrition is effected by the sole influence of a vital power inherent in the cells, and that the plasma is entirely passive. If the various tissues of the animal body, different as they are in their chemical constitution, obtain their nourishment from the protein- and fat-compounds of the plasma (which contains the elements of the cells, but not the different cellular substances themselves,) it is clear that the cells and tissues must produce a metamorphic effect on that portion of the nutriment which is homologous with themselves. Their catalytic, or as Schwann<sup>2</sup>, in his theory of cells, terms it, their metabolic power, evolves from the plasma the materials that serve for the nutrition of the cells. The plasma is here the cyto-blastema, the catalytic or metabolic force lies in the cells and tissues. But although the plasma acts only passively in this nutritive process, we cannot deny it a peculiar vital power. This is first manifested in the formation of the cyto-blastema, for the force that creates these forms cannot be regarded as independent of the plasma. If the nucleus is formed by the solidification of fibrin in the plasma, which from the similarity of their constitution is probable, its formation must be regarded as the result of a purely plastic force in the liquor sanguinis. If, however, all the different portions of the body,—the muscles, bones, cartilages, horny matter, serous membranes, sinews, neurilema, brain, &c.,—are nourished and formed by the protein- and fat-compounds of the plasma, we must arrange these compounds into those which *are*, and those which *are not*, homologous to the tissues. Neither albumen, fibrin, nor fat can belong to the second division, since the tissues are formed from these substances.

I have already mentioned, that those constituents of the plasma, that are excreted in the urine and the sweat, cannot reasonably be considered as any longer nutritious, for it would be at variance with our ideas of a consistent organization to suppose that substances which could be subservient to the preservation of the body should be removed from it; it would be just as irrational to conceive that they were conveyed into the body in order to circulate therein, with the nutriment, with no definite object; it only remains then for us to conclude that

<sup>2</sup> Mikroskopische Untersuchungen, p. 231 and 234.

they are formed in the body, and in that case they can only be regarded as products of metamorphosis. The most important constituents of the secretions and excretions separated from the blood are urea, uric acid, bilin, hæmaphæin, biliphæin, extractive matters, lactic acid, salts, and mucus. Mucus must not, however, be regarded as a genuine excretion, for it plays an important part in the animal organism, and its removal is not a matter of vital necessity, but the urea, uric acid, and bilin are chemical combinations which, in a healthy condition of the system, are removed by certain organs in a fixed quantity, but which are not met with in the blood itself: and, indeed, it is difficult to understand how these products of the metamorphosis of the plasma (constant in their amount, and determinate in their composition) are produced in the formation of tissues, which present entirely different chemical characters, and which are frequently developed in very changeable proportions. It seems more rational to conceive that the urea, uric acid, and bilin are products of the metamorphosis of a substance of a fixed chemical composition, which, by the simplicity and uniformity of the changes to which it is subjected, gives origin to the formation of these products of decomposition. We shall revert to this subject in our observations on the metamorphosis of the blood-corpuscles, and on the manner in which the production of hæmaphæin may be explained.

There still remain for our consideration the extractive matters, the lactic acid of the urine, and the salts: all these substances occur in no inconsiderable quantity in the blood, and their formation during the act of nutrition of the various tissues is consequently very probable. If the various tissues are formed from the plasma of the blood, and if, as is probably the case, their formation is accompanied by the absorption of oxygen and the liberation of carbon, the resulting products may be extremely various: indeed there are so many different forms of extractive matter, of the true nature of which we are still ignorant, that we are justified in the conclusion, that they undergo very complicated transformations during the nutrition of the tissues. While all the tissues may be considered as albuminous, gelatinous, osseous, horny, or fatty, it must be remembered that the various fats differ materially in their constitution, and that there are similar differences amongst the



albuminous tissues. If we regard the extractive matters as the products of the nutrition and waste of the different tissues, the variety in which they exhibit themselves is not at variance with the conceptions we are led to form respecting the nature of metamorphosis. Another circumstance in support of this view is, that the formation of similar matters is observed in the vegetable kingdom, where there is a vital, reciprocal action between the cells and the nutriment, combined either with the production of lactic, or of some allied acid. Although these extractive matters are, without doubt, entirely different from those that occur in the animal body, they correspond in many of their physical and chemical properties: both are incapable of being exhibited in a crystalline form, they dissolve readily in water and partially in alcohol, they are precipitated by many of the metallic oxides, and it is a matter of extreme difficulty to obtain them in a state of purity in consequence of their tendency to undergo transformation and to become chemically changed.

Until the extractive matters of the animal body have been accurately analysed, and the composition of the various tissues has been determined, it will be impossible to obtain a rational insight into the nature of these changes.

It appears from the statements of Berzelius, as well as from my own investigations, that some of the extractive matters which occur in the blood and in the flesh are also met with in the urine. It still remains to be decided whether all the extractive matters of the flesh pass unchanged into the blood and are thrown off by the urine, or whether they become changed in their passage; or, lastly, whether they are not partially metamorphosed in certain organs, and again rendered fit to serve the purposes of nutrition. When we consider the wisdom that is universally obvious in the economy of the animal body, it seems probable that the last is the most correct view, and it is by no means improbable that the gelatinous tissues are sustained by a cytoblastema, allied to the extractive matters. The fact that some of the extractive matters of flesh are not only strengthening but very digestible, renders it more than probable that some of the matters of this class serve as nourishment; while others, incompatible with the purposes of nutrition, are excreted.

The plasma of the blood contains salts, some of which are peculiar to that fluid, and are transmitted from thence into the secretions and excretions, while others (especially the phosphates of lime and magnesia, fluoride of calcium, together with small quantities of the sulphates and carbonates of soda and lime), occur in the bones as actual constituents of the body. The latter are conveyed into the body with the food, partly in the state of phosphates, &c., while their formation is also in part due to the production of phosphoric and sulphuric acids by oxydation of the phosphorus and sulphur which occur in the protein-compounds, and the subsequent combination of those acids with bases. These salts are again found in the urine, for they are removed by the blood during the metamorphosis of the bones, and are excreted by the kidneys. In the present state of our chemical knowledge, it is impossible to assign with certainty any definite function, to the large quantity of salts, which enters the blood but is not transferred into any of the solid textures of the body. Hewson suggested that the object of the saline constituents of the serum was to enable the blood-corpuscles to retain their discoid form. Albumen, without salts, has as little power as pure water in hindering the solution of the blood-corpuscles. Hewson's view seems to be supported by the facts, that the alkaline salts which occur in only a very slight proportion in solid textures, are found in a very large quantity in the blood; and further, that when water is mixed with blood, by injection into a vein, in a sufficiently large quantity to dissolve or modify the form of the corpuscles, a fatal result ensues. As these salts are continuously introduced into the blood with the food, a corresponding amount must be removed by the excretions. The salts have, however, other functions than that assigned to them by Hewson. The blood, as is well known, has always an alkaline reaction, and it might therefore be supposed that if a large quantity of an acid were taken, the reaction of the blood would be neutralized. This is, however, by no means the case, partly because only a certain quantity of the acid enters the blood, the remainder being carried off by the intestinal canal, and partly because the portion that does enter the circulating fluid is at once removed by the kidneys. Thus all the mineral acids may be detected in the urine after their administration; the vegetable acids appear, however, to undergo

a partial change, at least Wöhler found that neutral potash, or soda salts, formed by a vegetable acid, were decomposed in the organism, and that the bases were removed by the urine in the form of carbonates. We thus see that the existence of basic salts in the blood is indispensably necessary; and as neutral or acid salts are usually contained in the food, it is clear that they must undergo such a change in the body as to permit of the removal of the acids by the urine while the bases are retained.

There is every reason to suppose that the basic salts of potash and soda in the blood serve for the purpose of combining with the lactic, fatty, uric, and probably carbonic acids that are continually secreted during metamorphosis.

The salts of lactic and uric acid are in part excreted in that form; and in part, as has been remarked, are decomposed, so that the free acids are separated by the kidneys, while the bases are retained. The salts of the fatty acids appear to be secreted only in the liver. Whether chloride of sodium, which appears to be requisite for all the mammalia, serves merely for the purpose of preventing the solution of the blood-corpuscles, or whether it does not, like some other salts, act as a stimulant on the nerves, and in that manner influence the composition of the blood, is a question not easily answered.

#### *Active metamorphosis of the blood.*

As the plasma is subjected to a continuous change in the peripheral system during the nutrition of the tissues, it becomes a matter of necessity that it should also receive a continuous supply. This is afforded to it by the chyle, a fluid generally only poorly supplied with blood-corpuscles, but abounding (at least at certain times) in lymph- and chyle-corpuscles, and oil-vesicles, and containing some fibrin. The chyle is therefore not blood, although closely allied to it; if, however, as is generally believed, the chyle is the only nutriment of the blood, it must ultimately be changed into blood, and this transformation is effected by an increase of the blood-corpuscles, and by a diminution of the lymph-, chyle-, and fat-corpuscles, while the fibrin is not only increased, but becomes more plastic. A change must therefore take place in the blood itself, and this must be not of a passive nature, as during nutrition in the peripheral system, but active; we must assume that there is a formation and de-

velopment of certain substances in the blood, produced by a certain vital power inherent in this fluid, with the aid of necessary potential forces, as, for instance, of oxygen. This change or metamorphosis represents the real vitality of the blood, and, as far as we at present understand it, we may describe it as a process in which not only blood-corpuscles are formed, (by a consumption of lymph-, chyle-, and fat-globules,) and fibrin is produced, but further, in which the blood-corpuscles are again consumed; for it is obvious that if there is a continuous process of formation while their total number remains nearly constant, there must be a corresponding consumption of them.

The presence of atmospheric oxygen is indispensably requisite for this active metamorphosis of the blood, and one of the results of this change is an excretion of carbon, which combines with a portion of the absorbed oxygen, so as to develop a certain degree of warmth. The probability that the chemical process, which occurs during nutrition in the peripheral system by means of the plasma, involves the absorption of oxygen, has been already noticed. The importance of the presence of oxygen for the perfect metamorphosis of the blood, and indeed for life itself, is sufficiently obvious from the circumstance that the cessation of the respiratory process is followed by immediate death.

Although the respiratory process is as necessary for the active metamorphosis of the blood as for the production of animal heat, yet neither of these processes is to be referred to the lungs alone, but to the whole peripheral system. If it were otherwise, the temperature of the lungs would be much higher than it actually is; whereas, in reality the excess of temperature of those organs is very slight, and may probably be sufficiently accounted for by the more energetic action of the atmospheric oxygen on the mass of the blood in these organs than in other parts of the body.

I cannot give any description of the manner in which the blood-corpuscles are formed from the consumption of lymph-, chyle-, and fat-corpuscles. Physiologists suppose that a capsule, which at first is very thin, but subsequently becomes thicker and thicker, is developed around the lymph-corpuscle: this capsule is filled with hæmatoglobulin, which at first is comparatively colourless, but subsequently assumes a vivid red tint. We are perfectly unable to state where the first hæmatoglobulin



is formed, but there is no doubt that the respiratory process is essential to its production.

Schultz and Henle have examined the blood-corpuscles in their various stages of development, and have arrived at very similar conclusions. Schultz<sup>1</sup> observed that the young corpuscles were poorer in colouring matter than the older ones, and that, consequently, the nucleus was much more distinct. The capsule becomes tumid in proportion to the age and development of the blood-corpuscle, whilst the nucleus becomes gradually smaller, and in some cases entirely disappears. Water acts very differently on blood-corpuscles in different stages of development. The younger and more delicate blood-corpuscles are quickly and readily dilated by a very small quantity of water; they are soon entirely deprived of their colouring matter, and become perfectly clear and transparent; whilst the older and more developed corpuscles entirely resist the action of water, or at the most only become rounded, and do not dissolve except on the addition of a large quantity of water. They remarked at the same time that the corpuscles most abundant in colouring matter frequently presented a minute nucleus up to their final disappearance; while many of the most highly developed ones gave no indications whatever of a nucleus.

That a metamorphosis of the blood-corpuscles does occur cannot be for a moment doubted, but with respect to the peculiar circumstances under which it is conducted, and to the products that are then formed, we know scarcely anything: all that we have been able to ascertain with any degree of certainty is, that oxygen is absorbed, and carbon given off during the process; and the following facts justify us in this conclusion:

*a.* Dark blood, both within the system and out of it, assumes a lively reddish tint on being brought in contact with oxygen. This change is probably based on a chemical change in the hæmatin.

*b.* Blood taken from the body and agitated with oxygen absorbs a certain portion of the gas, while carbonic acid is formed. The mere serum, however, which contains no blood-corpuscles, absorbs only a very little oxygen, and develops carbonic acid in a corresponding ratio.

<sup>1</sup> Ueber die gehemmte und gesteigerte Auflösung und Ausscheidung der verbrauchten Blutbläschen. Hufeland's Journal, 1838.

c. The consumption of oxygen and the formation of carbonic acid stand in a direct ratio with the amount of blood-corpuscles, and with the number of respirations in a given period.

Hence it is obvious that the oxygen taken up by the blood during the respiratory process, is, for the most part, consumed in the metamorphosis of the corpuscles.<sup>1</sup>

The development of the blood-corpuscles is doubtless conducted on the same principle as that of other cells; i. e. the blood-corpuscles exert a transforming influence on the surrounding plasma; they select from it the materials requisite for their development, and reject the non-homologous products that are formed in it. Amongst the matters that are taken up there must be always free oxygen.

During the later stages of development of the blood-corpus-

<sup>1</sup> [There are two rival theories respecting the manner in which oxygen is taken up by the blood and conveyed to the peripheral system. Liebig maintains that this is effected solely by the iron in the corpuscles, while Mulder refers it entirely to the oxidation of protein-compounds. Liebig asserts that the corpuscles of arterial blood contain peroxide of iron; that, in their passage through the capillaries, they lose a portion of their oxygen and combine with carbonic acid, so that, in the venous system, they no longer contain peroxide, but carbonate of the protoxide of iron. When they reach the lungs, an exchange takes place between the carbonic acid of the blood and the oxygen of the atmosphere. Mulder, on the other hand, denies that the blood-corpuscles are conveyers of oxygen, and that iron is oxidized during respiration, as assumed by Liebig, and he found his conclusions on the following grounds:

a. The iron is so intimately connected with the other elements of hæmatin that it cannot be removed, even by long digestion of this constituent in dilute hydrochloric or sulphuric acid. (Vide supra, p. 41.) Consequently it is highly improbable that it should be oxidized in the lungs. Liebig, indeed, observes that dilute acids remove iron from dried blood, but Mulder gets over this difficulty by showing that other constituents of the blood, besides the colouring matter, contain this metal, apparently in an oxidized state.

β. If, as Liebig asserts, peroxide of iron exists in arterial, and carbonate of protoxide of iron in venous blood, almost any dilute acid would be capable of extracting the oxide, which we have shown not to be the case.

γ. Assuming, with Liebig, that the iron exists in arterial blood as a peroxide, the organic part of hæmatin would be different; instead of being  $C_{44} H_{22} N_3 O_6$ , it would be  $2(C_4 H_{22} N_3 O_6 Fe) - Fe_2 O_3$ , or  $2(C_{44} H_{22} N_3 O_{4.5})$ .

δ. The probability of its existence in a metallic state has been already shown. (Vide supra, p. 42.)

ε. The amount of hæmatin in the whole mass of the blood is far too inconsiderable to carry a due supply of oxygen to the whole system.

Mulder's theory has been alluded to in an early part of this work. (Vide supra, p. 12, note.) We shall have occasion to notice it at some length in our observations on the differences between arterial and venous blood.]

cles up to their final solution, they must undergo so thorough a change as to leave no remains of their principal constituents, the hæmatoglobulin, the nuclei, and the capsules, for not a trace of these substances, is found either in the plasma or in any of the secreted or excreted fluids, in which we should naturally expect to find them. It is altogether impossible to state how this change takes place; this, however, is evident, that if the metamorphosis of the blood-corpuscles terminates in their perfect solution, both the capsule and the nucleus must be entirely dissolved, and neither hæmatin nor globulin can be contained in it at the moment of solution. What the products of this change actually are is very difficult to determine with any degree of certainty.

Transitory combinations with a brief existence may be produced, or compounds may be formed, which undergo a further decomposition in certain organs. It is very probable that substances closely resembling the extractive matters are formed in the metamorphosis of the blood-corpuscles, by the decomposition of which urea or uric acid are produced, so that by the influence of a certain organ (the kidney) the compound is separated into those substances, and another form of extractive matter. It may further be presumed that the composition of hæmaphæin is such as to include the constituents of biliphæin, and that the hepatic cells possess the power of secreting the biliphæin from it.

Combinations may likewise be formed of which we know actually nothing; for the blood has not yet been sufficiently examined. These points need not engross our consideration at present; and I will only remark, that in my attempt to prove that the fibrin and hæmaphæin of the plasma, the urea, uric acid, bilin and its acids, the biliphæin, and certain acid fats, are products of the metamorphosis of the blood-corpuscles, I by no means conclude that they are the *only* products; in fact, I freely grant my assent to the possibility of many others.

The blood contains a certain amount of fibrin, varying from .2 to .9, or according to Andral even to 1.0%, which on whipping is separated in thickish, globular, elastic, stringy masses; the chyle appears from my analyses to contain not more than from .02 to .04% of fibrin, which, in consequence of its slight tenacity separates on whipping into loose and

globular, or else into flocculent mucous masses. Fibrin is therefore obviously formed in the active metamorphosis of the blood; and that portion which preexists in the chyle is modified and rendered more plastic. It is a well-known fact that the respiratory process not only increases the plasticity of fibrin in the blood, but also its quantity, and that on the other hand the amount of fibrin diminishes in blood which is not efficiently brought in contact with oxygen. As the blood-corpuscles principally consume oxygen during their change, it appears very probable that the fibrin is produced during this process.

This view is elucidated, and I may say confirmed, by my analyses of the blood, in which it appears that with very few exceptions, the amount of fibrin always varies inversely with the mass of the blood-corpuscles, or, in other words, that the more corpuscles there are, the less in quantity is the fibrin, and *vice versa*. This fact is readily explained by the adoption of the view that fibrin is formed from the blood-corpuscles; for it is obvious that the quantity of fibrin in the plasma must increase during an extraordinary consumption of the corpuscles.

Let us now inquire which of the constituents of the blood-corpuscles has been employed in the production of that most essential ingredient of the plasma, the fibrin? It can hardly be the globulin, for that forms from 4 to 10% of the blood, and, being a protein-compound, is so intimately connected in its chemical relations to fibrin, that if we were to suppose that it were converted into fibrin, we should expect to meet with a much greater quantity of this latter constituent in the blood than we find actually existing; still less can it be the hæmatin; indeed, the use of this appears to be *to facilitate and to maintain the independent metamorphosis of the blood-corpuscles, through its energetic capacity for the absorption of oxygen, and through its own metamorphosis*, instead of forming a product for the further nutrition of the plasma. The capsules and the nuclei still remain for consideration. Of the former we know very little, but the latter actually possess chemical characters which approximate them to fibrin, so that there is no impediment to the supposition that this important constituent of the blood is formed from the nuclei by a metamorphic process, accompanied probably by the absorption of oxygen and the separation of carbon.



The nuclei may be distinctly seen in young blood-corpuscles, but in the process of development they become smaller, and, according to Schultz and Henle, as the final solution of the blood-corpuscles approaches, they altogether disappear; hence the metamorphosis of the nuclei is by no means sudden, but progresses with the development of the blood-corpuscles.

Burdach,<sup>1</sup> R. Wagner,<sup>2</sup> and Valentin<sup>3</sup> are of opinion, that as long as the blood-corpuscles circulate in the living body, they possess no nucleus, and that this is only formed at the instant that the blood-corpuscle is removed from the circulation. R. Wagner found that nuclei were formed by the mere contact of the blood-corpuscles with atmospheric air. This is a further point of analogy between the nuclei and the fibrin of the plasma; and if we could only succeed in observing the unequivocal reappearance of a nucleus in a blood-corpuscle removed from the body, and in which, on account of its advanced development, the nucleus had undergone solution, we might then, in my opinion, consider that the change of the nuclei into fibrin was sufficiently established, especially when we reflect that no other constituent of the blood possesses the extremely characteristic property of being retained in solution in living blood, and of separating into an insoluble mass as soon as the vitality of the fluid is destroyed.

If we assume that the fibrin is formed in this manner, it follows that the amount of fibrin must always stand in an inverse ratio to that of the blood-corpuscles; and this is in reality the case,—that whenever the activity of the metamorphosis is increased, the amount of fibrin must likewise increase; and further, that whenever the blood is hindered in its circulation, or its supply of oxygen is stopped or lessened, the amount of fibrin must diminish. All these consequences really take place. Blood that stagnates in the vessels loses fibrin, for it is consumed, while no fresh supply can be formed. Menstrual blood, and the blood in *menæna* contain no fibrin;<sup>4</sup> and I shall subsequently refer to other similar cases.

<sup>1</sup> Physiologie, vol. 4, pp. 27 and 94.

<sup>2</sup> Beiträge zur vergleichenden Physiologie des Blutes, 1838, p. 14.

<sup>3</sup> Handbuch der Entwicklungsgeschichte des Menschen, p. 296.

<sup>4</sup> [That the menstrual discharge does *occasionally* contain fibrin will be shown in a future part of this work.]

Let us now proceed with the metamorphosis of the blood-corpuscles; the next question for consideration is this: *What changes do the hæmatin and globulin undergo?* It has been already shown that both these substances must undergo an entire change during the period of development of the blood-corpuscles, that terminates in their consumption or solution. The plasma contains a peculiar colouring matter, hæmaphæin, to which it owes its yellowish colour,<sup>1</sup> and which cannot accumulate in it beyond a certain amount, because it is continuously removed by the kidneys; it is, in fact, this constituent that gives the yellow or yellowish-brown tint to the urine.

It can hardly be doubted that the hæmaphæin is a product of the metamorphosis of the hæmatin; especially, if it can be proved that it is formed solely from the blood-corpuscles, and that it is contained in them to a large amount. We can obtain from the serum only slight traces of hæmaphæin, but the clot yields a considerable amount of colouring matter, which must be therefore contained in the blood-corpuscles. The hæmaphæin is formed from the hæmatin during the development of the blood-corpuscles, and the change is probably accompanied by an absorption of oxygen and a separation of carbon; the youngest blood-corpuscles must consequently contain less hæmaphæin than those that are older; and when the act of development terminates in their solution, they no longer possess any hæmatin, but only hæmaphæin. In a normal state, the consumption and production of the blood-corpuscles must be nearly balanced, and consequently the proportion of the hæmatin to the hæmaphæin will remain tolerably constant; when the metamorphosis of the blood is accelerated (i. e. when the circulation is quickened, and the mutual action between the blood and oxygen is increased) more blood-corpuscles will be consumed in a given time than in the normal state, and the consumption will especially include the older ones which abound in colouring matter, and which in their development are approximating to the stage of solution.

<sup>1</sup> When the serum, after the separation of the clot, is of a reddish tint, which is not unfrequently the case, blood-corpuscles are suspended in it. In icterus the serum is often of a brownish red colour, in consequence of the presence of biliphæin; in this case the colour rapidly changes into a green, on the addition of nitric acid.

In these cases there is, therefore, not merely a diminution of the quantity of the blood-corpuscles, but likewise of the colouring matter contained therein, since the corpuscles that remain are young and deficient in colouring matter, containing, in addition to hæmatin, only a very small quantity of hæmaphæin. If the circulation of the blood is impeded in any part of the body, and it is prevented from receiving its due supply of oxygen, the metamorphosis will likewise be impeded and rendered imperfect; the matured blood-corpuscles which are approaching the stage of solution will not be dissolved, and there will consequently be an accumulation of colouring matter, especially of hæmaphæin, which is the most abundant pigment in the matured corpuscles.

All these appearances are actually observed. I shall be able to demonstrate that, in inflammatory affections, (when the metamorphosis of the blood is excited to increased activity in consequence of the accelerated circulation and the increased mutual action of the blood and oxygen,) there is only a small amount of colouring matter present in the blood, and that, in all probability, hæmaphæin constitutes but a minute portion of the little that does exist; while, on the other hand, in blood which is retained in the body without being submitted to the due action of oxygen, in which the perfect metamorphosis is checked, and the corpuscles are not dissolved, as in *melæna* and in *morbus maculosus*, there is a great excess of hæmaphæin. The colouring matter may also accumulate when organs that take an active part in the metamorphosis of the blood are affected, as I have observed in *morbus Brightii*.

I shall now proceed to show that it is much more probable that such substances as urea, uric acid, and bilin, which are definite compounds secreted in a nearly constant ratio by peculiar organs, should be products of the active metamorphosis of the blood-corpuscles, than that they should be formed during the metamorphosis of the plasma in connexion with the process of nutrition.

It is but reasonable to infer that such substances as urea, uric acid, and bilin, which are separated in large quantity by the kidneys and liver from the blood, should be products of the metamorphosis of a substance of an invariably uniform composition. In every class of animals, in the most varied forms of

existence, under the most opposite kinds of food, we find that the bile is a secretion of the liver; whilst amongst all the higher classes of animals and many of the lower, urea and uric acid, or one of the two, occur as a constant secretion of the kidney.<sup>1</sup> It seems opposed to all reason to imagine that in animals as different in structure as they are opposite in their habits of life, and under every possible variation of circumstances, these fixed and definite compounds should be products of the metamorphosis of the plasma during the nutrition of every form of tissue. It is, however, easy to conceive that the corpuscles which, although different in their form, are similar, if not identical, in their chemical constitution, in the blood of all these animals, should, under similar conditions, yield similar products as the result of their metamorphosis, and that these products should take the form of urea, uric acid, and bilin. This consideration alone is deserving of much weight in support of the view that I am now advocating. If the urea, uric acid, and bilin were formed in accordance with the other hypothesis, their production would be increased, diminished, or stopped, according as nutrition was proceeding favorably, was deficient, or was entirely checked, as happens in certain disorders. But it is well known that the production of these substances is by no means dependent on such circumstances. The secretion of urea, uric acid, and bile proceeds, both in man and animals, when the tissues are gradually wasting from disease, and when their nutrition is utterly suspended; they are separated long after the body has ceased to take any food whatever, in fact, as long as respiration and even life itself remains, the only necessary condition being the healthy state of the secreting organs. I have had several opportunities of examining the urine during inflammatory diseases, both before and during, or shortly after the height of the attack, and have found that, in the latter case, there was always a greater amount of urea than in the former. This is easily explained by the consideration that the active metamorphosis of the blood-corpuscles is accelerated by an excited inflammatory state, and that, consequently, a larger number of the corpuscles is consumed during a given time, than in the ordinary condition of the system.

<sup>1</sup> Müller's Handbuch der Physiologie, vol. 1, pp. 515 and 588.



My analyses of the blood are even more confirmatory than any of the preceding statements, of the production of these substances during the active metamorphosis of the corpuscles.

I analysed the blood of the aorta and vena renalis of one animal, and the blood of the vena portarum and vena hepatica of another animal, with the following results:<sup>1</sup>

1.	a. Blood of aorta, in 1000 parts.	b. Blood of vena renalis, in 1000 parts.
Water . . .	790·000	778·000
Solid constituents . .	210·000	222·000
Fibrin . . .	8·200	? <sup>2</sup>
Albumen . . .	90·300	99·230
2.	a. Blood of vena portarum.	b. Blood of vena hepatica.
Water . . .	738·000	725·000
Solid constituents . .	262·000	275·000
Fibrin . . .	3·500	2·500
Fat . . .	1·968	1·560
Albumen . . .	114·636	130·000
Globulin . . .	116·358	112·580
Hæmatin . . .	4·920	4·420
Hæmaphæin . . .	1·467	1·040
Extractive matter . .	16·236	17·160

Here we observe that the arterial blood contains more water than the blood of the renal vein, and that the blood of the vena portarum contains more than that of the vena hepatica; the arterial blood and the blood of the vena portarum contain a larger amount of fibrin than the blood from the renal and hepatic veins respectively. The blood of the renal vein contains more albumen and fewer blood-corpuscles than arterial blood, and a similar relation holds good between the blood of the hepatic vein and of the vena portarum. Passing over all other points of difference, the results at which we have already arrived afford an *à priori* argument for, and a confirmation of, my theory respecting the formation of urea, uric acid, and bile,

<sup>1</sup> In the first analysis, the venous blood from both the renal veins was collected. The amount, although small, was sufficient for the required purpose. Professor Gurlt, of our veterinary school, had the kindness to obtain the blood for me.

<sup>2</sup> The whole amount of blood from both renal veins did not exceed sixteen grains, a quantity not sufficiently large to admit of the determination of the fibrin by whipping. I employed it in determining the ratio of the albumen to the dried residue, and found that while the aortic blood contained 43, the blood of the renal veins contained 44·7% of albumen.

from the corpuscles during the active metamorphosis of the blood.

Since the kidneys and the liver secrete fluids from the blood of less specific gravity than the blood itself, it is clear that in its passage through these organs it must become richer in solid constituents than before it entered them; moreover, as in its circulation through these organs it meets with no free oxygen, it must be poorer in fibrin when it leaves them than on its entrance.

The change that the blood undergoes in these organs, is, however, by no means so simple as it might appear to be, and as, in fact, these analyses might lead us to conceive. There result from it the products of the metamorphosis of the corpuscles, or of the compounds that are formed from them, as well as of the plasma, during the nutrition of these organs. The excess of albumen in the blood of the renal and hepatic veins is clearly opposed to the view that the urea and bilin are formed from the plasma.

It is sufficiently established that the renal cells possess the power of removing an excess of salts and water from the blood, in the same manner as the hepatic cells separate fat.

I beg expressly to repeat that I do not regard the urea, uric acid, and bilin, as the only substances that are formed, besides fibrin and hæmaphæin, during the active metamorphosis of the blood-corpuscles; on the contrary, I am of opinion that other substances are likewise produced, regarding the formation of which we might speak with greater certainty if almost everything regarding them were not based on mere conjectures. It is, for instance, very probable that a portion of the globulin is converted into albumen, which, since both substances are protein-compounds, might happen in two ways, either by a portion of the phosphorus, or sulphur, being oxydised, if globulin contain more of those elements than albumen; or if, on the other hand, it contain less, by the globulin dividing into, for instance, one half or one third of a protein-compound with all the phosphorus and sulphur, and into one half or two thirds of a protein-compound devoid of phosphorus and sulphur, which then undergoes further metamorphosis. The fat, which is more abundant in the blood-corpuscles than in the serum, must likewise undergo a change. The fat of the serum appears to be softer than that of the corpuscles, while that of the fibrin is firm and

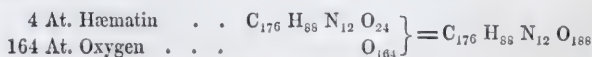
white. In all of them there is cholesterin, margaric and oleic acids. Berzelius could detect no phosphorus in the fat of fibrin ; neither did Lecanu find any in the fat of the serum. The fat containing phosphorus, which Boudet found in the blood, must belong to the corpuscles. We cannot form any very clear idea of the manner in which these metamorphoses are conducted ; it is, however, probable that the phosphorized fats are conducted to the brain. Since the fats that are taken as food consist, for the most part, of stearin, margarin, and olein, it would appear as if fatty acids were formed from them by a process of oxydation during the succeeding formation of blood-corpuscles, and the consumption of lymph-, chyle-, and oil-globules.

The elementary composition of many of the substances that are formed from the blood, and of some that occur in it, are known to us, but of the greater number of the matters that are produced during its metamorphosis, particularly of the extractive matters, we are entirely ignorant.

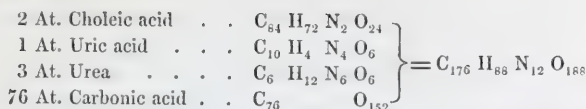
The extremely high atomic numbers of many of these substances, as, for instance, of the protein-compounds, renders it very probable that each atom is decomposed into various new atoms of less atomic weight. We are, however, at present entirely deficient in many of the requisite data, in our knowledge regarding the connecting links, as, for instance, of the composition of the extractive matters, of the different tissues, &c., without which even a superficial insight into the nature of the metamorphosis of the blood cannot possibly be obtained.

With the scanty materials in our possession, we may nevertheless attempt an ideal sketch of the metamorphic action that goes on in the blood, the conditions being that there is an absorption of oxygen, and that carbon is given off ; it will, at any rate, afford an illustration of the facility with which such equations may be deduced, and of the slight degree of confidence that should be placed on their interpretation, unless they are tested by established facts.

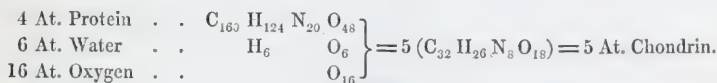
We may, for instance, suppose that 4 equiv. of the organic portion of hæmatin ( $C_{44} H_{22} N_3 O_6$ ), by the absorption of oxygen, will be decomposed into choleic acid, uric acid, urea, and carbonic acid. Thus—



Likewise,



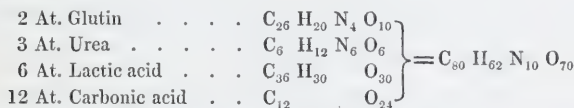
We can also show how chondrin may be supposed to be formed from protein by the addition of oxygen and hydrogen : for,



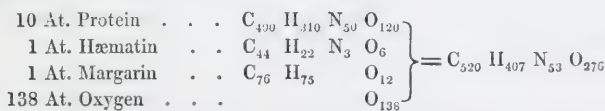
We may, in a similar manner, conceive that gluten, urea, and lactic acid are formed from protein by the absorption of oxygen, and the liberation of carbonic acid ; for



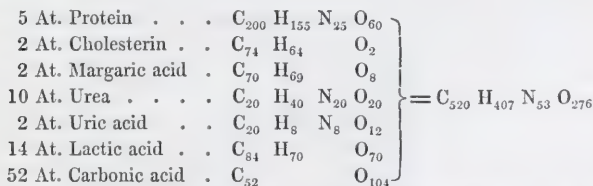
Likewise,



If we conceive that the blood-corpuscles are formed of globulin (a protein-compound), hæmatin, and margarin, they may, by the absorption of oxygen and the development of carbonic acid, be decomposed into many other substances, as, for instance, into protein, cholesterin, margarinic acid, urea, uric acid, and lactic acid ; for,



Likewise,



Many similar illustrations of possible metamorphic actions might be adduced ; but, as they do not contribute to the advancement of chemical science, we shall omit to notice them.



## 2. Special chemistry of the blood.

*Proximate constituents of the blood.*

The blood is a fluid of a very complicated nature, and has been proved to include the following constituents in man and in certain mammalia :

	Water.
Protein-compounds . .	{ Fibrin.
	{ Albumen.
	{ Globulin.
Colouring matters . .	{ Hæmatin.
	{ Hæmaphæin.
Extractive matters . .	{ Alcohol-extract.
	{ Spirit-extract.
	{ Water-extract.
	{ Cholesterin.
	{ Serolin.
Fats . . . . .	{ Red and white solid fats, containing phosphorus.
	{ Margarinic acid.
	{ Oleic acid.
	{ Iron (peroxide.)
	{ Albuminate of soda.
	{ Phosphates of lime, magnesia, and soda.
	{ Sulphate of potash.
Salts . . . . .	{ Carbonates of lime, magnesia, and soda.
	{ Chlorides of sodium and potassium.
	{ Lactate of soda.
	{ Oleate and margarate of soda.
Gases . . . . .	{ Oxygen.
	{ Nitrogen.
	{ Carbonic acid.
	{ Sulphur.
	{ Phosphorus.

Traces of the following substances have also been detected in the blood in certain pathological states of the system :

Sugar.  
 Urea.  
 Bilin and its acids (?).  
 Biliphaein.  
 Glutin (?).  
 Hæmacyanin.  
 Erythrogin.  
 Hydrochlorate of ammonia.  
 Acetate of soda.

Benzoate of soda.  
Margarin.  
Olein.  
Copper.  
Manganese.  
Silica.

*On the methods of analysing the blood.*

Although many of the proximate constituents of the blood may be recognized without difficulty, there are some (especially those which exist in only minute quantity) that cannot be readily detected. An exact quantitative analysis of the blood, including the determination of all the substances in the foregoing table, would, in the present state of chemistry, be almost an impossibility; we must, therefore, content ourselves with the quantitative determination of the *more important* constituents, and arrange and determine the others, as, for instance, the fats, salts, extractive matters, &c. in groups. For this purpose fresh blood must be used: the clot must be allowed to separate from the serum, and the two (the clot and the serum) must then be analysed separately.

The following method is given by Berzelius.<sup>1</sup> Two known quantities of blood are taken, one of which is allowed to coagulate spontaneously, while the other is evaporated for the purpose of ascertaining the quantity of water. The clot, when thoroughly separated, is removed from the first of these quantities, cut into pieces, and placed upon an open weighed filter, resting upon several folds of blotting paper; it must then be covered with a similar weighed filter, over which some more blotting paper must be placed, and the whole must be compressed by a stone or other weight. The blotting paper must be changed as long as any moisture is communicated to it, and the clot must be subsequently dried *in vacuo* over sulphuric acid, and carefully weighed. By deducting the known weight of the filters we obtain that of the fibrin and blood-corpuscles.

The dried clot must now be frequently washed with water at from 75° to 85°, until the fibrin is left colourless.

The dried blood which has been used for the purpose of ascertaining the quantity of water must be successively treated

<sup>1</sup> Thierchemie, p. 93.

with ether, alcohol, and boiling water. The ultimate residue consists of fibrin, blood-corpuscles, and albumen; by deducting the already determined weight of the fibrin and blood-corpuscles, we obtain the weight of the albumen. Ether takes up the fat; alcohol, certain extractive matters, and lactates; boiling water, certain extractive matters, chloride of sodium, &c. The serum (the quantitative relation of which to the clot is known) is gently boiled, by which means the albumen is coagulated, and all moisture is removed by evaporation.

The dried residue is pulverized and treated with boiling water, which leaves albumen and fat unacted upon; the latter of which may be now taken up by ether.

The water dissolves the salts, certain extractive matters, and some fat, or fatty-acid compounds.

The watery solution must now be evaporated, and the residue treated with alcohol, which takes up the chlorides of sodium and potassium, the lactates, extract of flesh, and perhaps some fat, if any happens to be present.

An objection may be raised against this method, that the separation of the blood-corpuscles from the serum is not sufficiently perfect.

The complete removal of the serum is a matter of very considerable difficulty, in consequence of the formation of a dried surface, at those parts of the clot which are in contact with the paper, by which means a check is opposed to the egress of any moisture from the interior portions. Indeed, the moist clot can only be perfectly freed from hæmatoglobulin with difficulty, and with the loss of some fibrin; if it were thoroughly dried, the difficulty would be confined to the washing out of the blood-corpuscles. But when fibrin remains for a considerable time in water, a small portion of it is dissolved, and a part of it is transformed into a viscid mass, consisting of very minute microscopic granules, which are not easily washed out. When all the blood-corpuscles are not inclosed by the coagulated fibrin, the serum assumes a reddish tint in consequence of their presence; they must then be taken into estimation with the serum. In most cases, analyses made in this manner would yield too high a number for the blood-corpuscles; in some few cases the assigned number would be too small.

Lecanu's method of analysing the blood is very similar to that of Berzelius.

Denis<sup>1</sup> adopts a method of analysing this fluid which involves considerable time and manipulation; and, after all, does not give results of very great accuracy.

Fresh blood is received into two vessels of known capacity, one of which is narrow and high. One portion is used for the determination of the water, the carbonate of soda, and the chlorides of sodium and potassium; the other for the estimation of the other constituents of the blood.

i. The first portion is evaporated to dryness in the water-bath, pulverized in an agate mortar, again heated on the water-bath, and the quantity of evaporated water estimated.

The residue is incinerated, digested in water, and filtered; the filtered solution is evaporated to dryness, and the residue is weighed, dissolved in water, and treated with nitrate of silver; chloride of silver, and oxide of silver (?) are precipitated. This precipitate is dissolved in nitric acid, the solution is evaporated and crystallized; the crystals are dissolved, decomposed, and neutralized by carbonate of soda. The solution which is thus obtained (of nitrate of soda) is filtered, evaporated to dryness, and incinerated with animal charcoal in a platinum crucible. It is then digested in water, and the carbonate of soda ascertained. Upon deducting the weight of the salt from that of the whole ash of the blood, we obtain as a residue the weight of the chlorides of sodium and potassium.

ii. The other portion is allowed to stand for twenty-four hours, in order to permit of the thorough separation of the clot from the serum.

The latter is removed with a pipette, and the separation is continued until incipient signs of decay present themselves. The water is removed from the serum, *in vacuo*, at a temperature of from 120° to 140°. The clot is placed in a small bag and washed with water until all the colouring matter is removed. The residue, consisting of fibrin, is then placed in the water that has been used for the washing of the clot. The fibrin is separated by decantation, the solution of colouring matter being carefully poured off. It is then washed with fresh water.

<sup>1</sup> Recherches expérimentales sur le Sang humain, considéré à l'état sain, par S. Denis: Paris, 1830, p. 121.



In the separation of the hæmatoglobulin from the fibrin, according to this method, about the seventieth part of the clot is lost in the water. The solution of the colouring matter is heated until the coagulation of the hæmatoglobulin is effected, which is then separated and freed from moisture by pressure.

The fluids are then evaporated to dryness. We have now four subdivisions:

- a.* The fibrin which still contains fat and cruorin.<sup>1</sup>
- b.* Albumen with cruorin, salts, and extractive matter.
- c.* Hæmatoglobulin with fat, extractive matter, and salts of iron and the earths.
- d.* The evaporated fluid separated from the hæmatoglobulin, containing salts and osmazome.

These four portions are dried, weighed, put into glass flasks, and submitted for some minutes to the action of alcohol of ·800—·820, at a temperature of 86°; they are then filtered, and the spirituous solutions united and evaporated. The residue, consisting of extractive matters and salts, must be incinerated, by which means the quantity of extractive matter is determined.

The four portions must now be treated with boiling water, by which cruorin and certain salts are removed.

The portions *a* and *d* are now combined, and the three are treated with boiling alcohol of ·800 for the purpose of extracting the fat. The filtered solutions are united and evaporated, and the cholesterin separated by crystallization from the fats which contain phosphorus. The mixed portion of *a* and *d* contains tolerably pure albumen; it is dried, weighed, and incinerated, and the ash is preserved.

The second portion contains fibrin; this likewise is incinerated, and the ash added to the former.

Lastly, the hæmatoglobulin is dried, weighed, and incinerated. The collected ashes are analysed with regard to the proportions of peroxide of iron, phosphates of lime and magnesia, &c.

<sup>1</sup> Denis applies the term *cruorin* to a substance obtained by boiling fibrin and albumen in water. It is soluble in water, insoluble in alcohol and ether, of an agreeable taste, and precipitable by tannic acid. It appears to be produced by the action of the boiling water on fibrin previously affected by long contact with water.

This method is objectionable, not merely on account of the time and labour required for its various stages, but further, because the whole of the water cannot be estimated by the indicated process. Moreover, the quantity of the hæmatoglobulin which is dependent upon the quantity of blood-corpuscles, will be given in excess, as it is certain that the whole of the serum cannot be separated from the clot, in the manner proposed by Denis. The determination of the fibrin may also be inaccurate in consequence of the continuous treatment of the clot with water, which has the effect of transforming a portion of it (*i. e.* the fibrin) into minute flocculi or granules which combine with a viscid substance. The estimation of the fat and of the extractive matters is also very inaccurate; the quantity of fat given by Denis in his analyses being much too large, and of extractive matter, too small. Finally, no certain results with respect to the separation of the salts can be obtained by this method. Whatever may be the faults of his process, he is at least deserving of praise for having conducted no less than eighty-three analyses in this laborious manner.

The method that I pursue in the analysis of the blood, if not strictly correct, at least gives results that approximate nearer to the truth than those of Denis. In explaining it, I must enter a little into detail, in order to indicate certain necessary precautions, and to explain on what points it is deficient.

*a.* I receive two, three, or at the most four ounces of blood, as it flows from the vein, in a thin glass, and stir it,<sup>1</sup> but not violently, till the fibrin separates. If it be stirred too violently, a portion of the fibrin becomes separated in the form of finely-divided scum, which cannot be easily collected. When the blood has completely cooled, it is weighed, together with the rod and glass, in a good balance; it is then poured out, the glass is cleansed and dried, the rod is freed from the adherent fibrin, and is washed and dried: the glass and rod are then weighed, and the quantity of blood determined.

*b.* Any fibrin that separates in flocculi from the blood must be collected, added to the former, pressed, and placed in water. If the water become strongly coloured, it must be poured off

<sup>1</sup> [A bunch of fine twigs is generally used for this purpose, but the fibrin may be obtained with as much accuracy by shaking the blood in a stoppered bottle containing a few fragments of lead, to which it readily adheres.]

and renewed until the fibrin is found to be colourless, which is usually the case in from 18 to 24 hours. It is almost needless to mention that none of the flocculi of fibrin must be allowed to escape when we pour off the water. The decolorized fibrin is dried, cautiously broken up, pulverized in an evaporating basin, and then submitted to a temperature of  $230^{\circ}$  until it ceases to lose weight.<sup>1</sup> It is then weighed. It is again finely triturated, placed in a flask and heated, first with anhydrous alcohol, and then with ether, for the purpose of extracting the whole of the fat. The ether and alcohol must be evaporated in the water-bath, and the weight of the fat estimated. The quantity of fibrin and of fat associated with it must then be calculated in regard to the whole quantity of the blood.

*c.* A quantity varying from 30 to 50 grains of defibrinated blood must be accurately weighed in a small basin, and cautiously heated over the flame of a spirit-lamp. This portion must then be triturated, submitted to the action of the water-bath, pulverized as completely as possible, and the heat continued until it ceases to lose weight. Lastly, it must be heated in a chloride of zinc bath to  $230^{\circ}$ . The loss of weight indicates the quantity of water.

*d.* An optional quantity (say from 400 to 600 grains) of defibrinated blood, must be boiled over the flame of a spirit-lamp, in order to coagulate the whole of the albumen, and subsequently placed on the water-bath for the purpose of removing all moisture. As soon as the blood has become sufficiently dry to admit of being partially broken up, it must be carefully triturated in a mortar, and then again placed on the water-bath. All the tough coriaceous portions, which are not easily pulverizable, must be carefully removed: by further drying they become gelatinous, tough, and ultimately brittle. The powdered blood ought, however, if the previous steps have been properly exe-

<sup>1</sup> I may observe that, in my analyses of blood, I always use small porcelain basins, weighing from 200 to 300 grains, and that I pulverize dried substances in the basins themselves with a small pestle. As these substances, when thoroughly dry and warm, are apt to exhibit a strong electrical repulsion of their particles, it is advisable to place the basin on a sheet of glazed paper, by which precaution any portion that may escape from it can be easily replaced. Any particles adhering to the fingers or to the pestle may be swept off with a soft feather. The most scrupulous exactness and accuracy is requisite in these investigations.



cuted, to assume a flocculent and bright-red appearance, even before it is perfectly dried, and should not exhibit any dark, glittering particles under the process of trituration. If it is black, or of a bad colour, brittle, very tough, and extremely difficult to triturate, it is not fit for the purpose of analysis.

*e.* This flocculent powder must be reduced to dryness (the trituration being at the same time kept up), and a small portion (8, 10, or at most 15 grains) weighed in a glass flask for further experiments. If the powder should appear to contain moisture, a small quantity (for instance about 8 grains) may be submitted to a temperature of  $230^{\circ}$  for a short time, and the whole error from this source may be thus estimated.

I have found that when the powdered blood has been submitted to too strong or too continuous a heat, the spirit-extract is only imperfectly taken up: hence it may be advisable not to reduce the whole of the powder to a state of absolute dryness, but rather to calculate from a small portion the quantity of retained moisture.

This powder must now be treated with a little anhydrous alcohol. Some ether must then be poured over it, and it must be heated to the boiling point, in order to dissolve the fat as thoroughly as possible.<sup>1</sup>

After the deposition of the powder the clear ether must be poured off, and the operation repeated two or three times. The ethereal solutions are then collected, the ether evaporated, and the residual fat submitted for a short time to a heat of  $212^{\circ}$ , and then weighed.

*f.* The powdered blood, thus freed from fat, must now (after

<sup>1</sup> I use small and very thin glass flasks, containing from one and a half to two ounces (which, like all other apparatus, may be obtained from the establishment of Hoffmann and Eberhardt, of Berlin): at first I pour on the pulverized blood only about twice its volume of alcohol; I then heat the flask on the sand-bath, keeping it in almost continuous motion, in order that none of it may spirt over, until it boils; I then add a considerable quantity of ether, which precipitates the salts dissolved in the alcohol, so that nothing but fat remains in solution. If too much alcohol has been added, some of the salts remain dissolved, and the apparent weight of the fat is increased. If ether alone be used for the extraction of the fat, the process must be repeated five or six times; the ether should be heated in boiling water just removed from the fire. In using dilute spirit for the purpose of extraction, I heat the flask over the flame of a spirit-lamp. In both cases the flask must be kept in continual motion, in order to regulate the ebullition.



the ether has been removed by evaporation) be boiled in the same flask with spirit<sup>1</sup> of .925—.935. This must be effected by gently moving the flask over the flame of a spirit-lamp. The spirituous solution must be allowed to boil freely for some time. All the constituents of the blood are taken up except the albumen: for the salts, extractive matters, hæmaphæin, and hæmatoglobulin are all soluble in boiling spirit of .935. The finely-divided albumen is gradually deposited from the clear, hot, deep-red solution, which becomes turbid on cooling. On carefully examining a thin section or stratum of the fluid, the presence of albumen or of deposited hæmatoglobulin in suspension, may be readily detected. In the first case, in addition to flocculi of a larger or smaller size, there are fine, clearly-defined points to be seen. If the spirituous solution be too thick and consistent to allow of the free deposition of the suspended albumen, the fluid must be cautiously decanted from the sediment into a large glass, and about double the quantity of spirit of .935 added. It must be heated until all the hæmatoglobulin is dissolved, and then gradually cooled. When the solution is perfectly cold, we find deposited at the bottom a small quantity of separated albumen, which must be again washed with alcohol into the flask. The residue in the flask must be boiled with spirit of .935 as long as any additional colouring matter is given off: five, six, or even eight boilings are requisite. What now remains is albumen. If the hæmatin has been removed as completely as possible, the albumen, while moist, appears of a grayish-green, and when dried, of a dirty-gray colour; and leaves on incineration a bright yellow residue, containing traces of peroxide of iron. It must be washed out of the flask with a little water, with the aid of a feather; the water must be removed by evaporation upon the water-bath, and the residue submitted to a temperature of 230°, and weighed.

*g.* The spirituous solutions are collected in a glass, and usually throw down a certain quantity of hæmatoglobulin, in the form of flocculi. After the decantation of the fluid, they must be dried upon the water-bath, triturated as finely as possible, rubbed with warm water to a uniform pulp, and washed with spirit of .925. They must be added to the flocculi, of which we shall speak directly. As much alcohol is now added

<sup>1</sup> I mix equal parts of alcohol of 85 or 90° with distilled water.

as is sufficient to precipitate the dissolved hæmatoglobulin in distinct flocks. If the whole is now allowed to stand for 12—18 hours, all these flocks will be deposited at the bottom of the vessel, and there will remain above them a clear yellow fluid, which must be removed with a syphon, and the last remaining portion with a pipette. The flocks must be washed two or three times with fresh spirit of from .89 to .90, which must be removed by the same means.

If these spirituous solutions are of a yellow or citron colour, we may assume that they contain only salts and extractive matters tinged with hæmaphæin: if they are of a reddish tint, then hæmatoglobulin is also present, which must be precipitated by the addition of stronger spirit.

We have now to analyse (I) the flocculi, and (II) the spirituous solution.

1. *a.* One or two ounces of alcohol of .83 or .80 (the stronger the better) are poured over the flocks; the mixture is then well stirred, and a sufficient quantity (usually from three to eight drops) of dilute sulphuric acid is added *guttatim*, until a decided change of colour of the flocks is observed. The flocks are now allowed to settle, and the deep red alcoholic solution is decanted. The decolorized flocks are then treated with pure alcohol until they cease to give off any more colouring matter. If, *after this*, the flocks have still a reddish tinge, they must be treated with a little more acidulated alcohol. If the flocks are as free from hæmatin as possible, they assume a more or less clearly defined gray colour; when dried, they appear as a dirty-gray powder, and on incineration they leave a yellow or orange-coloured ash.

*b.* The flocks must be washed with alcohol until they cease to exhibit an acid reaction; they must then be washed out of the glass flask (with the aid of a feather and a little water) into a porcelain basin, be dried first upon the water-bath, and subsequently at a temperature of 230°, and then weighed. They are estimated as globulin.

*c.* The red alcoholic solutions are mixed and saturated with ammonia to such an extent as to emit a decided ammoniacal odour; they are allowed to stand for some hours, in order to allow of the separation of the sulphate of ammonia;

they are then filtered, the sulphate is washed with a little alcohol, and the alcohol is subsequently evaporated. The residue consists of hæmatin with hæmaphæin, a trace of fat, and perhaps a little sulphate of ammonia. The latter may be taken up by water, at the risk, however, of losing an almost unappreciable trace of hæmaphæin, which is so far soluble in that fluid, as to communicate a yellow tint to it.

d. There may be certain cases in which the perfect separation of the two colouring matters, the hæmatin and hæmaphæin, would be a matter of considerable importance.

In all those cases in which I have found a large proportion of hæmatin, as in the blood in Bright's disease, and in menstrual blood, a certain portion of hæmaphæin is always associated with it. The dark coloured blood of melæna contains a peculiarly large quantity of hæmaphæin. The separation of the two colouring principles is best effected by alcohol, which dissolves the hæmaphæin, but not the hæmatin. The alcohol should be warmed, but not allowed to boil. Upon the evaporation of the alcohol the hæmaphæin is obtained, and when thoroughly dried, may be weighed.

II. a. By the evaporation of the alcoholic solutions, we obtain a yellow or brown residue, which has a saltish taste, and smells of extractive matters. It must be thoroughly dried, and then weighed.

b. If we wish to carry the analysis further, a known weight of the residue must be incinerated. The quantity of ash from 8 to 16 grains of this residue, will be small, probably from .3 to 1.0 grain. The residue likewise contains sugar, urea, and the colouring matter of the bile; the former may sometimes be detected by the taste, and the presence of the biliphæin may be recognized by the dark colour that it imparts to the serum. In so minute a quantity of material the urea cannot be easily traced.

In my analyses of the blood, I have always followed this course, and I feel convinced that if all necessary precautions are taken, the results will be nearer the truth than those obtained by any previously described method. I do not, however, intend to assert that my method will give *exactly accurate* results; and I shall at once proceed to point out,—

- 1, Those errors against which we may guard by caution ; and
- 2, Those which, with all care, cannot be avoided.

*Water.* This constituent may be determined with perfect exactness.

*Fibrin.* If the blood be whipt with due care, the fibrin is obtained as a thick, coriaceous, fibrous mass, surrounding the twigs of the rod. It can be removed without loss, and can be easily and quickly washed.

If it be stirred too rapidly, a portion of the fibrin becomes minutely subdivided, and after washing cannot be collected without some loss ; on the contrary, if it be stirred too slowly, or not long enough, the fibrin incloses many blood-corpuscles, and must either lie for some time in water, during which it is liable to a certain degree of change, or else it must be triturated and broken up, which induces the formation of flocks and of a viscid matter, and occasions considerable loss.

With a little experience and practice, the fibrin may be determined with great exactness. It is necessary to submit the dried fibrin to a temperature of  $230^{\circ}$ .

*Fat.* The fat contained in the fibrin may be estimated with great accuracy. It is only necessary to boil the pulverized fibrin with ether, or (which is better) with a mixture of ether and anhydrous alcohol, for four, five, or six times. The determination of the quantity of fat in the dried pulverized blood is much less certain and accurate. In an analysis in which I separated the hæmaphæin, I treated a large quantity of pulverized blood, six successive times with boiling ether, in a retort ; yet I still found a considerable quantity of fat in the hæmatin. This may be due, partly to the compounds of margaric and oleic acids becoming decomposed by the sulphuric acid in the alcohol during the boiling of the powdered blood which had been treated with ether ; and partly, I believe, to a little free fat which had not been taken up by the ether.

The fat appears to be extracted most perfectly when the powdered blood has been first loosened, as it were, with anhydrous alcohol. A quantity of ether, just sufficient to precipitate the salts dissolved by the alcohol, must then be added.



We may safely calculate that the whole of the free fat has been taken up, after six or seven extractions with ether. If, afterwards, the hæmatin should still be found to contain fat, some of the fatty acids must have been present, and acted upon by the acidified alcohol.

*Albumen.* Errors may arise in the determination of the albumen. These may be due, in the first place, to want of care in drying and pulverizing the blood. If the powdered blood has been allowed to dry into a cracked, brittle, tough, hard mass, which can only be repulverized with difficulty, and usually with considerable loss, then, only a portion of the hæmatoglobulin is taken up by the spirit, some of it now appearing of a yellow or gray-green colour, while another part of it occurs in the form of coarse black fragments, resisting the action of alcohol. This albumen has a somewhat red tint, and upon incineration leaves an ash, which is tolerably rich in iron.

Another source of error may lie in the spirit, which may be either too strong or too weak. I have always found a mixture of equal parts of alcohol of 85—90%, and of water, succeed best. I have occasionally found that with all precautions, and after boiling the residue with spirit until no more hæmatoglobulin was taken up, the albumen has still retained its red tint, and left an ash abounding in iron. I have never been able to ascertain the reason why diluted boiling alcohol should occasionally fail in the perfect extraction of the hæmatoglobulin.

If, after continuous boiling with dilute alcohol, the albumen still retains a red tint, I heat it with alcohol of .80—.82, in the same flask, and during ebullition I gradually add one, two, or even four drops of dilute sulphuric acid. The alcohol, at first colourless, now assumes a red tint, and the albumen, which is deposited upon standing, is either free from colour, or becomes so after being once more boiled in strong alcohol. It must then be boiled several times in alcohol of 0.925, which takes up the sulphate of globulin, and leaves the albumen.<sup>1</sup>

<sup>1</sup> As sulphate of albumen is insoluble in alcohol, we need not be apprehensive of losing any albumen by this extraction. I have convinced myself, by a special investigation, that spirit of .925 takes up nothing but sulphate of globulin from the pulverized residue of the blood. The fluid, while hot, is perfectly clear, but becomes rather turbid on cooling, in consequence of the separation of fat.

The alcoholic solution of the sulphate of hæmatin which (unless the alcohol were too dilute) contains no globulin, may be poured into a flask, and united with the fluid, which is subsequently obtained on the separation of the hæmatin from the globulin. (I, c.)

The sulphate of globulin separates pretty completely in the form of flocks from its alcoholic solution, on cooling. The supernatant spirit, which frequently has a slightly acid reaction, must be evaporated, till only a little is left; and we must then try whether upon the addition of strong alcohol, any globulin will still be precipitated. The whole of the sulphate of globulin must be added to that which is subsequently obtained from the hæmatoglobulin.

If, in accordance with the methods of Berzelius and Denis, the clot is washed for the purpose of obtaining the fibrin, the nuclei and capsules of the blood-corpuscles are entangled in, and increase the apparent quantity of the fibrin; if however the fibrin is removed by whipping, according to my method, then the nuclei and capsules remain in the albumen, and increase *its estimated* quantity.

I am not acquainted with any researches tending to show the degree in which the proportions of albumen and fibrin are modified by the adoption of one or other of these methods. Maitland,<sup>1</sup> however, observes that the quantity of fibrin obtained by whipping is less than that obtained by washing the clot. Müller,<sup>2</sup> on the contrary, thinks that the weight of the nuclei must be extremely small, and that the results obtained by the two methods are very nearly the same. My own opinion is, that the fibrin cannot be determined with accuracy from the washed clot.

*Globulin.* The globulin can be calculated with considerable accuracy if the albumen has been perfectly freed from the hæmatoglobulin. I have never yet succeeded in entirely removing the hæmatin from the globulin. It is known that even nearly colourless globulin leaves, on incineration, an ash which is pretty rich in peroxide of iron. Whether globulin generally contains peroxide of iron or not, I cannot positively

<sup>1</sup> An Experimental Essay on the Physiology of the Blood, 1838.

<sup>2</sup> Physiologie des Menschen, vol. 1, p. 119.

state. The globulin usually occurs in analyses of the blood as a sulphate, and as such I have always estimated it. It is of a grayish-white colour, forms a brownish solution in water, and on incineration leaves an ash, more or less abundant in iron.

If after the separation of hæmatin (in the manner already described), and after being washed in alcohol, the globulin retains a red tint, it must be again treated with a lukewarm mixture of sulphuric acid and alcohol, as before, which dissolves the hæmatin that had remained attached to the globulin. It must then be repeatedly washed with alcohol, until it no longer exhibits any acid reaction.

*Hæmatin.* From the remarks which have been made respecting the albumen and the globulin, the reader may conclude that the hæmatin cannot always be determined with exactness; I conceive, however, that with all due care, the error in the determination of the hæmatin should be very trifling in 100 parts. It by no means necessarily follows that hæmatoglobulin should under all circumstances contain a constant proportion of hæmatin. Moreover, if the fat has not been previously entirely removed, a certain quantity may be associated with the hæmatin. If the hæmaphæin is separated from the hæmatin by means of warm alcohol, the fat dissolves simultaneously with the former of these colouring matters, and remains closely connected with it. If the alcohol used for the separation of the hæmatin from the globulin is not sufficiently strong; and if, after the saturation of the sulphuric acid with ammonia, a sufficient time is not allowed for the sulphate of ammonia to separate, a portion of this salt will pass through the filter, and become mixed with the hæmatin upon the evaporation of the alcohol. If this is the case, the salt may be easily recognized in the hæmatin by its crystalline form; and it must be extracted with water. It is always advisable to use strong alcohol, and to allow the saturated solution to stand for some hours before it is filtered.

*Hæmaphæin.* The determination of this constituent is somewhat uncertain and difficult, on account of the minute proportion in which it exists. It is occasionally found to

constitute only 0·1% of the weight of the dried blood. A portion of this colouring matter is taken up with the extractive matters from which we cannot separate it; another portion may be lost if the alcohol used for the separation of the hæmatin from the globulin is not of sufficient strength. In this case, on saturating with ammonia, a sulphate of ammonia is precipitated, and its removal is associated with a further loss of hæmaphæin. The hæmaphæin always retains a little fat.

*Salts and extractive matters.* These substances, with due caution and experience, may be determined with considerable accuracy. They must be separated from the hæmatoglobulin by the addition of dilute spirit, and to ensure a tolerably perfect separation, the whole should be allowed to stand from eighteen to twenty-four hours. I have already mentioned the course that must be adopted in case any of the hæmatoglobulin should be retained in the alcoholic solution. If the extractive matters and salts are evaporated on the water-bath to a slight residue, and then treated with anhydrous alcohol, the alcohol-extract will be dissolved and may be estimated. I do not know how to separate hæmaphæin from the extractive matters. In order to determine the salts, the extractive matters must be incinerated. By treating the (incinerated) residue with hot alcohol of ·85, we take up the chloride of sodium. The residue must be dissolved in a little water, and rendered neutral by the addition of acetic acid. The acetates of potash and soda may now be taken up by alcohol. These salts correspond with the lactates.<sup>1</sup> There still remain the

<sup>1</sup> [The existence of lactic acid and the lactates in the animal fluids is denied *in toto* by the Giessen school.]

Enderlin's conclusions regarding the recently incinerated ash of blood may be summed up in the following terms:

1. The ash does not effervesce on the addition of an acid.
  2. Hot water poured on the ash becomes alkaline; it holds in solution alkaline phosphates and sulphates, chloride of sodium, and sometimes chloride of potassium, but no other salts.
- a.* On the addition of a neutral solution of nitrate of silver to this fluid, there is a yellow precipitate, which is partly soluble in nitric acid; a portion, however, consisting of chloride of silver, remaining undissolved. The addition of nitric acid causes no effervescence. On neutralizing the acid filtrate with ammonia, a yellow precipitate of tribasic phosphate of silver ( $3\text{AgO}, \text{PO}_5$ ) is thrown down.
- b.* On treating the aqueous solution of the ash with a solution of chloride of cal-



phosphates and sulphates of lime, magnesia, potash, and soda. If they are dissolved in a little dilute nitric acid, the addition of ammonia induces the precipitation of the earthy phosphates, while the other salts remain in solution.

There are some substances occurring only in very minute quantities, or in certain diseased states, which cannot be always easily detected.

1. *Urea*. This substance has never yet been observed in any great quantity in the blood.

I have detected a minute quantity of urea in the blood of a healthy calf. I allowed the blood (about fifteen or sixteen pounds) to run into a vessel filled with alcohol, and assiduously stirred the mixture. The alcohol was removed by pressure, evaporated, and the residue extracted with anhydrous alcohol. After filtration, and a second evaporation, the residue was again dissolved in a little anhydrous alcohol, and the bases of the lactates and fatty acids precipitated with sulphuric acid. The filtered liquid was digested with carbonate of baryta, evaporated, dissolved in water, the fats and fatty acids removed by filtration, the aqueous solution concentrated, and nitric acid added. The greater part of the fluid was removed by being placed *in vacuo* over strong sulphuric acid; alcohol was poured over the residue, and the

cium, there is a copious gelatinous precipitate of phosphate of lime ( $3\text{CaO}, \text{PO}_5$ ), which dissolves in nitric acid without effervescence. On treating this acid solution with nitrate of silver, and neutralizing with ammonia, the tribasic phosphate of silver is precipitated as before. The addition of the chloride of calcium neutralizes the previously alkaline fluid.

From 1, we see that the alkaline reaction is not due to the presence of alkaline carbonates; and 2 shows it is not dependent on the presence of free potash or soda, for otherwise the fluid would not be neutralized by the chloride of calcium. Hence the albumen in the blood cannot exist as a soda-compound (albuminate of soda); neither can there be alkaline lactates, acetates, nor fatty-acid salts in that fluid; and on the above grounds, Enderlin conceives that we are justified in assuming that the alkaline reaction of the ash is dependent on the presence of tribasic phosphate of soda ( $3\text{NaO}, \text{PO}_5$ ); and as this is the only salt that remains tribasic at a red heat, he concludes that the alkalinity of the blood, as well as of the ash, is dependent on it. Enderlin is the only chemist who excludes carbonates from the ash of the blood and other animal fluids. The manner in which he accounts for the occurrence of these salts in the analyses of other chemists is very plausible. On exposing  $3\text{NaO}, \text{PO}_5$  to the atmosphere, it becomes converted into  $2\text{NaO}, \text{HIO}, \text{PO}_5$  and  $\text{NaO}, \text{CO}_2$ . (Liebig and Wöhler's *Annalen der Chemie und Pharmacie*; March 1844.)]

solution submitted to spontaneous evaporation. The microscope then revealed the presence of nitrate of urea, which was recognized by its peculiar crystalline form.

[Marchand got only slight microscopic indications of urea from twenty pounds of the serum of the blood of a healthy cow; and as the urine of that animal contains a larger amount of urea (4% according to Sprengel) than that of man, the blood must likewise contain a larger proportion of this ingredient. He calculates (assuming that there are twenty pounds of blood in a man's body, and that one ounce and a half of urea is eliminated in twenty-four hours) that the blood contains only the 15,360th part of its weight of urea, a quantity that could hardly be determined analytically, if it were increased thirty-fold.<sup>1</sup>]

After the extirpation of the kidneys, and in Bright's disease, it has been found in so large a proportion that its detection is accomplished with comparative ease. My method, in looking for urea, is to treat a certain quantity of the blood with alcohol for the purpose of throwing down the protein-compounds; then to filter; and, subsequently, to wash the residue upon the filter with alcohol. The alcoholic solution (including the washings of the filter) must be evaporated to a small residue, and treated with anhydrous alcohol. The solution is decanted from the spirit-extract, which remains undissolved, is evaporated, and again treated with anhydrous alcohol. This process must, if necessary, be repeated until the residue is freely soluble in this menstruum.

The alcohol must then be evaporated, and the residue dissolved in water, which usually becomes slightly turbid in consequence of the separation of traces of fat. This fat is not easily separated by filtration; if, however, this process is determined upon, a considerable quantity of water is added; it is heated, and allowed to stand for some time. The watery solution will then pass through the filter tolerably clear, but slowly. It must be evaporated to a small residue, thoroughly cooled, and nitric acid then added. If the quantity of urea is not too minute, there are formed almost instantaneously an immense number of glittering crystalline scales. If the quantity of urea

<sup>1</sup> [That there is a peculiar difficulty in the precise determination of this constituent is shown by an experiment in which Marchand mixed one grain of urea with 200 of serum. He could only recover .2 of a grain.]

is *very minute*, the crystallized nitrate of urea may not be perceptible for several hours, and even then probably not without the aid of the microscope. In order to avoid any errors that might arise through the crystalline form of other salts, I first made myself thoroughly acquainted with the appearance presented under the microscope by alcohol-extract of urine (containing urea) when treated with nitric acid; then with the appearance presented by alcohol-extract of blood to which a little urine had been added, on the addition of nitric acid; then with that of alcohol-extract of blood devoid of urea; and, lastly, with blood which contains urea in the natural proportions. In this manner I found that the salt which most commonly occurs in the alcohol-extract of blood, the lactate of soda, may be readily distinguished under the microscope from the nitrate of urea, and that very minute quantities of urea may be detected with certainty.

Small quantities of urea may be recognized, by the peculiar and characteristic form of the nitrate, in fluids containing those extractive matters and salts of urine or of blood that are soluble in anhydrous alcohol. The forms which are principally and most frequently observed are depicted in fig. 3: *a* represents the characteristic crystalline form of nitrate of urea; *b*, *c*, *d*, *e*, groups that are formed in a somewhat dilute solution of urea; *f*, groups that are formed in a very dilute solution, chiefly at the edge of the fluid. Fig. 4 exhibits the crystalline form which is produced by the addition of nitric acid to the alcohol-extract of blood, containing no urea. These crystals are not perceptible until the fluid is evaporated nearly to dryness. Fig. 5 shows the form of the nitrate of urea in blood containing a considerable quantity of urea. I have several times observed these appearances in Bright's disease. With a little practice the commencement of the crystallization of the nitrate may be perceived; it begins by exhibiting an appearance of numerous fine parallel lines or streaks.

Oxalic acid may likewise be used in microscopic researches regarding the presence of urea in the blood. I have always, however, preferred the use of nitric acid, because, in the first place, it is not itself capable of crystallization as oxalic acid is; and, secondly, because the nitrates of potash and soda are much more soluble than the corresponding oxalates. Fig. 6 shows

the crystalline form of the oxalate of urea when alcohol-extract of urine, not very rich in urea, is treated with oxalic acid. In *a*, we see the characteristic crystalline form of the oxalate of urea; *b*, represents various groups of it. If the alcohol-extract of blood containing no urea be similarly treated, the crystals of fig. 7 are produced. Lastly, fig. 8 shows the crystals of oxalic acid itself, which are very similar to those of pure crystallized urea.

On treating the extractive matter of blood containing no urea with nitric acid, I have occasionally perceived crystals which, at first sight, appeared extremely similar to those of nitrate of urea, but which were in reality composed of nitrate of soda. These crystals are exhibited in fig. 9. They possess a very remarkable degree of thickness,<sup>1</sup> which I have endeavoured to represent in the plate. They may be distinguished from the similar form of nitrate of urea, by the circumstance that the former are not at all soluble in anhydrous alcohol, while the latter are readily dissolved in it. If nitrate of urea be present, it will recrystallize from its alcoholic solution in groups similar to those in fig. 10.

2. *Sugar*. This substance, which I once discovered in the blood of a calf, is very seldom to be found in healthy blood, although in certain pathological states, especially in diabetes mellitus, it has frequently been detected. If the quantity be very small, its presence is not always easily recognized. It is found mixed with the extractive matters, if the blood is analysed according to my directions, and if it exists in any quantity, may be recognized by the taste. If only a very little sugar be present, it is advisable to precipitate the protein-compounds from a large quantity of blood, with spirit. The fluid must then be filtered and evaporated to a small residue, which must be treated with anhydrous alcohol. The sugar, if present, must be taken up by the alcohol. If, after due evaporation, the residue have a sweetish taste, a portion of the sugar may be obtained tolerably pure, since its quantity cannot be very inconsiderable. With this view we dissolve it in a little water, add alcohol of '833, and allow it to stand for some time; under

<sup>1</sup> This is easily seen by slightly varying the focus.



favorable circumstances, a portion of the sugar will crystallize. In consequence of its intimate mixture with a large quantity of extractive matter, an exact quantitative analysis of the sugar is extremely difficult. The best method is that of fermentation, and estimating the quantity of carbonic acid that is formed. If the quantity of sugar be very minute, it cannot be recognized by the tongue, in consequence of the sweetness being disguised by the taste of the salts and extractive matter; it may, however, in this case, be detected by sulphuric acid, although this test is fallacious in the hands of unpractised analysts. The method to be pursued in this case is the same as that previously indicated; the spirituous solution must be evaporated, treated with anhydrous alcohol, and the fluid decanted. The precipitate which contains extractive matter, chloride of sodium, lactate of soda, and sugar, must be dissolved in water; and if (as is frequently the case) any hæmatoglobulin remains undissolved, the fluid must be filtered. The filtered fluid must be evaporated to dryness in a porcelain basin, on the water-bath, and one or two drops of dilute sulphuric acid (one part of acid to six of water) must be dropped upon the dried residue. On again submitting it to the heat of the water-bath, it is observed that those points which have been moistened by the acid at first assume a blue or violet tint, become gradually darker, and ultimately coal-black. When the quantity of sugar is very small, the colour is only sufficiently marked at the margin of the drop, or at points where the layer of extractive matter happens to be particularly thick. Unfortunately for the success of this test, a dark spot, varying from a deep brown to a dark dirty-violet tinge, but never positively black, is produced in the same manner in the spirit-extract of blood, which contains no sugar; so that, without a well-practised eye, it is difficult to decide upon the absence or presence of sugar by this test. After the addition of one grain of diabetic sugar in solution, to 500 grains of blood, (which contained no sugar,) no decided sweetness could be observed in the spirit-extract. The sulphuric acid test indicated the presence of sugar by the formation of a coal-black spot; on the addition of the acid to a portion of the extract of the same blood in which there was no sugar, a dirty violet spot was produced. In examining the blood of diabetic patients I once found so large a proportion of

sugar that it was readily detected by the taste ; on another occasion, however, it was only rendered manifest on the addition of sulphuric acid. But of all the tests for sugar in the blood, Trommer's is certainly the best. The protein-compounds are first precipitated with anhydrous alcohol, and dry carbonate of potash is then added to the filtered spirituous solution, which must be well shaken. On the addition of a little solution of sulphate of copper, and the application of heat, we observe, if sugar be present, a yellow or yellowish brown tint developed, produced by the reduction of the copper to a state of suboxide.

3. *Bile*. In healthy blood we find neither bilin nor biliphæin. In icterus we meet with biliphæin in the serum, which is more or less deeply coloured in proportion to the quantity of this pigment contained in it. It may be of a deep orange, or almost red colour, so as to lead to the suspicion of the presence of hæmatin in a state of solution. I found the serum nearly blood-red in a case of icterus ; but on shaking it against the sides of the vessel, the thin adhering layer appeared of a beautiful saffron colour. A similar colour was induced by the addition of water to the serum.

If only so small a quantity of biliphæin be present as to colour the serum slightly, it may be recognized by the addition of nitric acid, which produces a variety of tints, more or less green in their character. The albumen is at the same time precipitated in white flocks, upon which a slight tinge of green may be distinctly perceived.<sup>1</sup> In the deep red serum already alluded to, the addition of nitric acid produced an intensely clear grass-green colour, which, at some points, passed into a blue, and, in the course of twenty-four hours, into a yellow tint. The quantity of biliphæin varies directly with the intensity of the colour of the serum, and with the time required for the disappearance of the green tint, produced by the addition of nitric acid. Neither in the blood already alluded to, nor in another specimen which contained less biliphæin, could I discover a trace of bilin. The alcohol-extract of the blood had a saltish, but

<sup>1</sup> [In consequence of the facility with which coagulated albumen assumes a green tint under these conditions, we are often enabled to detect biliphæin (that would be otherwise unappreciable) in non-albuminous fluids, by the addition of a little albumen.]

not a bitter taste. I am not aware that bilin or bilifellinic acid<sup>1</sup> has ever been observed in the blood, and I hardly believe that they will be found, owing either to their not being taken up by the blood at all, or else to their speedy elimination by the urine. A large quantity of bilin would have a very dangerous effect upon the blood, since (as we have already shown) it dissolves the blood-corpuscles. I treated 500 grains of blood with half a grain of inspissated ox-bile, and then precipitated the protein-compounds with spirit, evaporated the fluid, and treated the residue with anhydrous alcohol. It is clear that the bile must be contained in this residue. After the evaporation of the alcohol, there remained a rather dark-coloured extract, having a bitter bile-like taste, and which, when dissolved in water, and nitric acid was added, manifested a slight green tinge. If, therefore, the bilin should constitute one-thousandth part of the blood, it would be easily detectible.

If the analysis of the fats and of the extractive matters is to be thoroughly carried out, (as in many cases it certainly ought to be,) much larger quantities of blood must be taken than I have made use of.

The various fats, however, as well as the different extractive matters, are at present too little known to enable us to attempt exact, or even approximating quantitative analyses.

4. *Fats.* Boudet<sup>2</sup> has analysed the fats which are taken up by alcohol from dried blood, after all substances that could be extracted by water have been removed. The alcoholic solution deposits serolin on cooling, which must be separated, and the alcohol evaporated. There remains as a residue a mixture of several fats, which were separated by Boudet in the following manner. Cold alcohol of .833 leaves undissolved a crystalline fat which contains phosphorus, and is apparently similar to the brain-fat, denominated *cerebrot* by Couerbe. Cholesterin is deposited by the spontaneous evaporation of the cold alcoholic solution; and on further evaporation, (after the removal of the cholesterin,) there is left a mixture of oleic and margarinic acids,

<sup>1</sup> [Enderlin states that he has detected minute quantities of choleate of soda (pure bile, according to Demarçay's theory) on three occasions, in the blood of calves and oxen. (*Annales der Chemie und Pharmacie*, April 1844.)]

<sup>2</sup> *Annal. de Chim. et de Phys.*, vol. 52, p. 337.

as well as some oleate and margarate of potash. In addition to these fats, there are certain coloured phosphorized and nitrogenous fats, similar probably to those which have been described by Couerbe, as *cephalot* and *eleencephol*. Lecanu found, in the fat of the serum, only cholesterin, serolin, margaric and oleic acids; he could detect no phosphorized fat. Berzelius<sup>1</sup> describes the fat of the fibrin, which may be taken up either by alcohol or ether, as solid and crystalline; when melted, of a yellow or light brown colour, readily soluble in cold alcohol, to which it imparts an acid reaction, indicating the presence of one or more of the fatty acids. Upon burning it, no acid ash is left.

Denis,<sup>2</sup> on the other hand, obtains from fibrin, as well as from albumen and hæmatoglobulin, a red phosphorized fat, which has an alkaline reaction. By digestion in caustic potash, a part is dissolved, while an insoluble portion remains, in the form of a white, saponified powder, readily soluble in ether, from which it may be again obtained, by spontaneous evaporation, in the form of delicate crystals, which burn like fat.

The portion of saponified fat which is dissolved in the potash must be precipitated by hydrochloric acid, and cannot be melted in the acid fluid, even on raising the temperature to a boiling heat. After having been removed by filtration, it is found to be soluble in alcohol and ether, and we may obtain it, after evaporating the fluid in which it is dissolved, as a fat, which becomes fluid at a temperature of 97°—104°, but is solid at an ordinary temperature. It has an acid reaction, and swells up, but is only very partially soluble in boiling water, from which, on evaporation, we obtain it (the dissolved portion) as a sort of film or coating.

According to Berzelius, it is similar to the acid salts of stearic and oleic acids described by Chevreul; it differs from them, however, by its greater solubility in ether and cold alcohol.

5. *Extractive matters.* These substances have been less carefully analysed than the fats, and the proportions in which they occur, are so small, that even in the analysis of a large quantity

<sup>1</sup> Thierchemie, p. 88.

<sup>2</sup> Recherches Expérimentales, &c. p. 101.



of blood, their exact determination is no easy matter. All that is known upon the subject is already given in the Introduction.

[A simple method of determining some of the most important constituents of the blood has been recently given by Figuier. It is based on the fact, made known many years ago by Berzelius, that after the addition of a solution of a neutral salt to defibrinated blood, the globules do not (as before) pass through filtering paper. On the addition of two parts of a solution of sulphate of soda of spec. grav. 1.130 to one of blood, Figuier found that the whole of the corpuscles remained on the surface of the filter. The following are the steps of his analysis. The fibrin is removed by whipping, dried, and weighed; the weight of the corpuscles is ascertained by the method indicated; and that of the albumen by coagulating, by means of heat, the filtered solution. The proportion of water is determined by evaporating a small known weight of the blood.]

*Analysis of coagulated blood.*

It sometimes happens that we receive blood for analysis that has already coagulated. The process to be adopted in such cases, although not in reality more difficult, involves a greater amount of chemical manipulation than when the fibrin is separated by whipping; and it appears to give less exact results.

The directions that I shall now give for the analysis of coagulated blood were published in a paper of mine some time ago;<sup>1</sup> I have, however, only once adopted this method, as I always prefer analysing the blood directly it is taken from the body.

The whole of the blood must first be weighed as accurately as possible, the clot must then be removed, and if sufficiently consistent, dried between folds of blotting paper, and then weighed. A portion of the clot (from 40 to 80 grains) is cut off, and its weight accurately taken; it is then thoroughly dried, and the loss of weight, which indicates the quantity of water, ascertained: the dried residue must be reduced to a spongy, bright-red fine powder, and treated with ether in order to remove the fat: it must subsequently be treated with boiling

<sup>1</sup> Brande's Archiv, vol. 28.

alcohol of .925 until the spirit ceases to take up any additional colouring matter, and the powder which remains has a dirty-gray or gray-green colour. This must be thoroughly dried, and estimated as *fibrin* and *albumen*. The reddened alcoholic solution, A, is set aside for further operation.

Another portion of the clot must be weighed and placed in a porcelain mortar, which should be provided with a pestle of such a size as exactly to fill it. Moreover, the edge of the mortar should be about one third of an inch above the head of the pestle. By this arrangement none of the clot can be lost. It must be reduced to a fine pulp, which must be treated with water until the flocculi of fibrin become perfectly white: these must be carefully collected and dried.

By the subtraction of the weight of the fibrin from that of the former residue, we obtain the weight of the albumen.

Before analysing the serum, it must be well shaken in order to render its constitution uniform; a portion must then be weighed, coagulated at a boiling heat, thoroughly dried, again weighed, and the proportion of water thus estimated. The dried residue must be finely pulverized, the fat removed by ether, and it must be then boiled with alcohol of .925 until everything which is soluble in that fluid has been taken up.

The residue consists of albumen, which must be dried and weighed. The alcoholic solution must be added to the solution A, and these mixed fluids analysed for the globulin, hæmatin, hæmaphæin, extractive matters and salts, in exactly the same manner as described in page 175.

#### ON THE HEALTHY BLOOD IN RELATION TO PHYSIOLOGY.

*(From my own analyses.)*

It is almost unnecessary to observe that the blood of one and the same individual may vary in its constitution at different times, and under different circumstances. We shall proceed to investigate the causes upon which these variations depend.

Amongst the most obvious causes we may place the proper supply, or the absence of sufficient nutrition.

The blood will clearly abound in water, in proportion to the quantity of fluid with which it is supplied; it will abound in

albuminous constituents, in fats, and salts, in proportion to the richness of the nutriment that has been taken, and of the chyle that has been evolved from that nutriment. In order to counteract the evils that might arise from an excess of water in the blood, (which, if allowed to remain unchecked, would induce too rapid a solution of the blood-corpuscles,) the kidneys, skin, and lungs exert an active agency; while, on the contrary, if there be a deficiency in the proportion of the water, caused either by too great exhalation, dependent upon excessive fatigue, or by a direct accumulation of the salts (which might impede the solution of the corpuscles) it is immediately indicated by an urgent desire for drink.

When substances, injurious to life, are taken into the stomach, only small quantities enter the blood, the great proportion being usually carried off by the intestinal canal, and by the organs of excretion and secretion. If the organism be unequal to the task of rejecting the injurious agent, the equilibrium of the system is destroyed, and death ensues.

Another cause of the varying nature of the blood, interesting equally to the physiologist and the physician, may be referred to the modifications that it undergoes in the nutrition of the organism, and to the changes undergone by the corpuscles, in connexion with the processes of secretion and excretion.

*On the distinctive characters of arterial and venous blood.*

The distinctive colours of arterial and venous blood are too well known to require any observation.<sup>1</sup>

<sup>1</sup> [From Scherer's experiments it appears that, when fresh red ox-blood is deprived of its fibrin and diluted with twice or thrice its volume of water, it assumes a dark venous tint, which is not affected by the passage of a current of oxygen through it. On the addition, however, of a little milk, oil, finely-powdered chalk or gypsum, the original bright red colour is evolved. These experiments are sufficient to prove that the bright red colour is dependent on other causes than oxidation, and that the dark venous tint does not arise from carbonic acid or carbon; in fact Scherer conceives that they prove that the former is dependent on the presence of white particles of chyle suspended in the fluid, an opinion confirmed by the microscope. It was observed by Hewson that, when the colour of the blood is bright red, the corpuscles are always biconcave; they reflect a large amount of light, and in this respect act as the chalk, milk, &c. in Scherer's experiments. When, on the other hand, the blood is of a dark colour, the corpuscles are biconvex, and the capsule is so thin as to admit o.

Arterial blood, on being whipt, allows the fibrin to separate in short conglobate masses, more tenacious and compact than the fibrin of venous blood.

The odour of arterial blood is considered to be stronger than that of venous. The temperature is also usually stated to be different, Jurine being the only experimentalist who assigns an equal temperature (i. e.  $102^{\circ}\cdot 2$ ) to both forms of blood. According to Scudamore the temperature of arterial blood in man is  $1^{\circ}\cdot 8$ , according to Kramer  $2^{\circ}\cdot 7$ , higher than venous blood. Dr. Davy found the difference in animals amount to  $3^{\circ}\cdot 6$ . The observations of Colemann, Cooper, and Martini are directly opposed to the above statement. (Lecanu, *Etudes chimiques sur le Sang*.)

The relative capacity for heat of arterial and venous blood is, according to Davy, as 839 to 852.

There is considerable difference of opinion among physiologists with respect to the specific gravity of arterial and venous blood: Hammerschmidt, Davy, Scudamore, and Letellier assert that the density of arterial is lower than that of venous blood; the former being represented by 1039·8—1042·9, the latter by 1053—1056.

the easy passage of the whole light through it; moreover, on account of its attenuation, it bursts, and allows of the escape of its contents, as may be observed on the addition of water to red blood. If the blood remain in contact with water till a dark tint becomes apparent, and a saturated solution of a neutral salt be then added, the corpuscles again become biconcave, in consequence of their being partially emptied by the endosmosis called into play by the different fluids within and without the capsule; and the capsules themselves, and the original bright red colour reappear. A current of carbonic acid gas passed through fresh red blood renders the corpuscles biconvex, and makes the blood assume a dark venous hue.

Mulder explains the difference between the colour of arterial and venous blood in the following manner: Two oxides of protein are formed in the act of respiration; they have a strong plastic tendency, and solidify round each corpuscle, making the capsule thicker and better qualified to reflect light. Each corpuscle of the arterialised blood is then in reality invested with a complete envelope of buffy coat, which gradually contracts, and speedily forms the cupped or biconcave surfaces, which, as we have already shown, are favorable to the reflection of light. On reaching the capillaries, the coating of the oxides of protein is removed, and the corpuscles, losing their opaque investment and their cupped form, can no longer reflect light, and the blood assumes a venous tint. (Mulder's *Versuch einer allgemeinen physiologischen Chemie*, pp. 344—59; or Dr. G. Bird's account of Mulder's Researches, in the *Medical Gazette*, December 1844.)



Boissier and Hamburger, on the contrary, found arterial denser than venous blood.

The observations of Bellingeri<sup>1</sup> respecting the electric relations of arterial and venous blood are very singular.

In birds, horses, and occasionally in sheep and calves, both forms of blood are in the same electric state. In other animals the arterial blood is positively electric in relation to the venous. The reverse has never been observed.

Observations have also been made regarding the comparative tendency to putrefaction of arterial and venous blood. Krimer and Kanig assert that arterial blood is the most prone to decay; Thackrah, on the contrary, makes a similar statement respecting venous blood.

In order to obtain any correct information with regard to the differences that undoubtedly exist in the composition of arterial and venous blood, it is necessary to have recourse to accurate chemical analyses. I have devoted much attention to this point, and fully concur with Schultz, Dumas and Prevost, and others, in the belief that the two forms of blood present marked differences of constitution.

I made use of the blood of horses in these experiments, and was kindly assisted by Professor Gurlt. The carotids, from which we obtained the arterial blood, were exposed, and opened in such a manner as to ensure the absence of any venous blood: the venous blood was obtained from the jugulars.

The analyses were made according to my ordinary method (*vide supra*), and gave the following results.<sup>2</sup>

1000 parts of blood contained:

	Analysis 1. Arterial blood.	Analysis 2. Venous blood.
Water . . . .	760.084	757.351
Solid residue . . . .	239.952	242.649
Fibrin . . . .	11.200	11.350
Fat . . . .	1.856	2.290
Albumen . . . .	78.880	85.875
Globulin . . . .	136.148	128.698
Hæmatin . . . .	4.872	5.176
Extractive matter and salts	6.960	9.160
100 parts of the blood-corpuscles contained 3.4 of hæmatin.		100 parts of the blood-corpuscles contained 3.9 of hæmatin.

<sup>1</sup> Quoted by Lecanu. *Etudes Chimiques sur le Sang humain*, p. 75.

<sup>2</sup> It must be observed that no sound horses were used for these experiments, but

The horse, which was suffering from malleus humidus, had taken its ordinary food up to the time of its death.

	Analysis 3. Arterial blood.	Analysis 4. Venous blood.
Water . . . .	789.390	786.506
Solid residue . . . .	210.610	213.494
Fibrin . . . .	6.050	5.080
Fat . . . .	1.320	1.456
Albumen . . . .	113.100	113.350
Globulin . . . .	76.400	78.040
Hæmatin . . . .	3.640	3.952
Extractive matter and salts	10.000	10.816
100 parts of blood-corpuscles contained 4.5 of hæmatin.		100 parts of blood-corpuscles contained 4.8 of hæmatin.

This was a meagre horse, killed in consequence of debility and old age.

From these analyses we are led to the conclusion that *arterial blood contains less solid residue generally than venous blood: it contains less fat, less albumen, less hæmatin, less extractive matters and salts than venous blood. The blood-corpuscles of arterial blood contain less colouring matter than those of venous blood.*

There does not appear to be any fixed relation between the fibrin and globulin (or, which is nearly the same thing, the mass of the blood-corpuscles,) in the contrasted analyses; for in Nos. 1 and 2 the fibrin in the venous exceeds that in the arterial blood, while in Nos. 3 and 4 we observe exactly the reverse. The same fluctuation is observable with respect to the globules, or the mass of the blood-corpuscles.

In an analysis of the blood of a healthy ox, made with the same object, I found the quantity of fibrin to be larger in the arterial than in the venous blood. In the former case it amounted to 4.90, and in the latter to only 4.82 in 1000 parts.

I shall now give the results obtained by other chemists upon this subject: I must, however, observe that their methods of analysis differ considerably from mine, and that I consider some of their results questionable.

only those intended for anatomical purposes. Some were too old and weak to be of any use; others were suffering from incurable disorders. Although it may be fairly questioned whether the composition of the blood in these animals is normal, the correctness of the comparative results must be unaffected as long as the lungs and other secreting and excreting organs remain healthy, provided there is no reason for supposing that the general metamorphosis of the blood is morbidly affected.

Denis analysed the blood of the hound. He found in 1000 parts :

	Arterial blood.	Venous blood.
Water . . . . .	830·0	830·0
Fibrin . . . . .	2·5	2·4
Albumen . . . . .	57·0	58·6
Hæmatoglobulin . . . . .	99·0	97·0
Extractive matter and salts . . . . .	11·0	12·0

In this instance both kinds of blood contain an equal proportion of solid residue : the former contains, as I have already observed in two out of three analyses, a larger quantity of fibrin. Denis found, as I have also done, that the quantity of albumen, and of extractive matters and salts, is less in arterial than in venous blood.

Hering<sup>1</sup> has analysed both kinds of blood in the bullock, the sheep, and the horse. In the blood of the bullock he found in 1000 parts :

	Arterial blood.	Venous blood.
Water . . . . .	798·9	794·9
Fibrin . . . . .	7·6	6·6
Albumen . . . . .	26·1	25·8
Hæmatoglobulin . . . . .	164·7	170·4
Extractive matter and salts . . . . .	2·7	2·3

In the blood of the sheep he found in 1000 parts :

	Arterial blood.	Venous blood.
Water . . . . .	850·2	841·2
Fibrin . . . . .	6·1	5·3
Albumen . . . . .	33·6	26·4
Hæmatoglobulin . . . . .	106·1	124·4
Extractive matter and salts . . . . .	4·0	2·7

In the blood of the horse he found in 1000 parts :

	Arterial blood.	Venous blood.
Water . . . . .	839·5	831·6
Fibrin . . . . .	4·6	6·9
Albumen . . . . .	22·0	26·7
Hæmatoglobulin . . . . .	130·0	131·1
Extractive matter and salts . . . . .	3·0	3·7

These analyses correspond very well with each other, and corroborate our remark that arterial leaves a smaller amount of

<sup>1</sup> Physiologie mit steter Berücksichtigung der Pathologie für Thierärzte. Stuttgart, 1832, p. 118.

solid residue than venous blood. In the bullock and sheep the fibrin in arterial exceeds that in venous blood; in the horse the reverse is observed. The same observation holds good with regard to the albumen, and in this respect (at least in the case of bullocks' and sheep's blood) Hering's results differ from those of Denis and myself.

Hering invariably found the quantity of blood-corpuscles to be greater in venous than in arterial blood; the proportion of extractive matters and salts are, however, extremely fluctuating.

Lecanu<sup>1</sup> has likewise analysed the blood of the horse, and found in 1000 parts:

	Blood of aorta.	Blood of vena cava descendens.
Water . . . . .	783·83	795·679
Blood-corpuscles . . .	122·68	106·759
Albumen with its salts, ex- tractive matter and salts }	93·49	97·562
	Blood of carotid.	Blood of jugular vein.
Water . . . . .	785·5	804·55
Blood-corpuscles . . .	125·6	111·03
Albumen with its salts, ex- tractive matter and salts }	88·9	84·45

These analyses differ from my own, and from those of Denis and Hering, in assigning to arterial a larger solid residue than to venous blood.

The quantity of blood-corpuscles is also greater in arterial than in venous blood, and Lecanu found the same to be the case with regard to the quantity of fibrin. The quantity of albumen fluctuated.

Schultz<sup>2</sup> observed that the venous blood of hungry and starving horses contained a larger amount of solid residue than the arterial, in the proportion of 186 to 155 in 1000 parts of blood: in a well-fed horse the reverse was the case, the solid residue of the arterial being to that of the venous blood, in the proportion of 229 to 195. The quantities of fibrin were very fluctuating: on one occasion the fibrin of the arterial was to the fibrin of the venous blood in the proportion of 5·3 to 8·1; on another occasion as 9·2 to 9·0. The hæmatoglobulin (which he considers identical with the colouring matter of the blood) was found to vary directly with the darkness of the blood's colour,

<sup>1</sup> Etudes chimiques sur le Sang humain. Paris, 1837, p. 83.

<sup>2</sup> System der Cirkulation, p. 138.



and consequently to be more abundant in venous than in arterial blood.<sup>1</sup> The reverse was the case with respect to the albumen.

Autenrieth, and Prevost and Dumas,<sup>2</sup> found a greater proportion of solid constituents in arterial than in venous blood : Lassaigne, like myself, found just the reverse : whilst Letellier asserts that there is no fixed rule on the subject.

Müller<sup>3</sup> and Berthold<sup>4</sup> observe that in the goat there is a larger proportion of fibrin in arterial than in venous blood : the latter chemist extends the statement to the blood of the cat and the sheep. The observations of Sigwart<sup>5</sup> and Lassaigne<sup>6</sup> are opposed to these statements.

Prevost and Dumas obtained from arterial a larger proportion of blood-corpuscles than from venous blood, and in this respect they confirm the observations of Lecanu and Denis. My own analyses, and those of Letellier, tend, however, to show that the proportion is a fluctuating one.

Hence we are led to the conclusion that there are certain differences in the composition of arterial and venous blood, which, however, are not constant, but vary according to circumstances.

The most important of these circumstances are the general health of the individual, and the mode of nourishment, whether dependent upon or independent of the health.

Let us now consider what must be the qualities of arterial and venous blood when all the functions of the organism are properly discharged, when the nutrition exactly corresponds with our actual wants, and when the blood undergoes the various changes that we have described in a former page.

Under these circumstances we arrive *à priori* at the conclusion that the final result of the changes in the blood during

<sup>1</sup> In order to avoid the error that might arise in the determination of the hæmatoglobulin from the retention of serum in the clot, Schultz proceeded in the following manner : He dried the clot, and subtracted from its residue the amount of solid matter left by a quantity of serum corresponding to the expelled moisture. The difference he regarded as hæmatoglobulin. We must not, however, forget that the hæmatoglobulin does not exist in a dry state in the blood ; and, further, that there are no grounds for assuming that the fluid in which it is held in solution is serum.

<sup>2</sup> Annales de Chimie et de Phys., vol. 13.

<sup>3</sup> Physiologie des Menschen, vol. 1, p. 119.

<sup>4</sup> Burdach's Physiologie, p. 281.

<sup>5</sup> Reil's Archiv, vol. 12, p. 5.

<sup>6</sup> Journal de Chimie Méd. vol. 1, p. 34.

the act of circulation must necessarily be this: there must be a substitution of fresh and proper nutriment to supply the place of those constituents of the blood which are being perpetually consumed; for it is obvious that if in each circulation the consumption of albumen or hæmatoglobulin exceeded the supply by the merest trace, after a certain period the blood would acquire an abnormal constitution. We know that albumen, fibrin, and salts are consumed in the nutrition of the peripheral system; if therefore the blood receives no fresh supply of these substances, before it arrives in the larger venous trunks, it is clear that the venous blood must be poorer in these substances than the arterial.

The blood also conveys away from the peripheral system various products formed by the consumption of the tissues; for instance, certain salts, extractive matters, &c., some of which are eliminated by the kidneys, in a state of great dilution, while others are removed by the skin. If the quantity removed exceed the supply, the venous blood will be poorer in extractive matters and salts than the arterial; it will be richer in these substances if the reverse be the case.

The venous blood will contain more or less water than the arterial, according as the elimination of water by the kidneys, liver, skin, and lungs, exceeds or is less than the quantity supplied by the fluid of nutrition.

The blood-corpuscles, and the germs from which they are developed, are likewise supplied to the blood by the nutrient fluids. They are further developed, and ultimately dissolved during the course of the circulation, and their development and solution is especially facilitated at those points where the action of oxygen on the blood is the most powerful.

It is obvious that the blood, immediately after having received the chyle, must contain more blood-corpuscles than before; it depends however upon several circumstances whether venous generally contains more or less corpuscles than arterial blood.

The plasma receives a supply of fibrin from the solution of the blood-corpuscles; if the supply exceeds the consumption of this constituent in the peripheral system, the venous blood may become richer in fibrin than the arterial.

If any albumen should be produced by the solution of the

blood-corpuscles, it may be regarded as a substitute for the portion of that constituent which has been taken up from the blood for the nourishment of the tissues.

From these observations we are led to conclude that there is no necessary variation in the composition of venous and arterial blood. The organism, when free from disturbing influences, possesses in itself various means of regulating the due admixture of its different juices, and more especially of that most important vital fluid, the blood.

Amongst these means we may place the influence of the nervous system, its power of increasing or lessening the action of the secreting and excreting organs, and of inducing in them either co-operating or vicarious action.

The differences in the constitution of arterial and venous blood cannot, however, by any possibility be very great. In my analyses they usually fluctuate between fractions of a hundredth part; and they appear to be less between analyses 3 and 4, than between analyses 1 and 2, since the former (anal. 3 and 4) were made on the blood of an old decrepid, half-starved horse, in which the change and waste of tissue, and the consequent metamorphosis of the blood, would be very slight. That the difference must be small is obvious, when we consider that the whole course of the circulation may be accomplished in 25-30 seconds; that the plasma just conveyed to the tissues must everywhere propel the nutrient matter conveyed there by the preceding blood-wave, and that the tissues, everywhere saturated with nutrient plasma, only take up a supply proportioned to their consumption. The process of nutrition in the peripheral system is continuous and is supported by the liquid plasma with which all the tissues are surcharged; hence these tissues become the temporary recipients of far more nutrient matter than they can possibly consume, even as the rivulet contains infinitely more water than is necessary for the refreshment of the soil on its banks.

In both cases we found that the venous blood contained a larger proportion of solid constituents than the arterial; hence we infer that more water was removed by means of the kidneys, liver, and skin, than had been supplied to the blood by the nutrient fluids.

The quantity of fibrin in the venous blood in analysis 2 is

greater than in the arterial blood, although, from our knowledge of the fact that fibrin is employed in the process of nutrition, we should have expected an opposite result. Hence we are led to attribute the excess of fibrin to the consumption of a large proportion of blood-corpuscles, a view which is confirmed by the circumstance that the venous blood in this instance is poorer in blood-corpuscles than the arterial.

The proportions are reversed in analysis 4, but whether from opposite causes or not, I cannot decide. It is singular that in both instances the quantity of albumen is greater in the venous than in the arterial blood, since there can be no doubt that this constituent is consumed in the nutrition of the tissues, and that a portion of the changed plasma enters the lymphatics. I do not see how this increase can be accounted for, unless we assume, as I have previously done, that a portion of the globulin of the blood-corpuscles is converted into albumen during their metamorphosis.

In the present state of our knowledge regarding the metamorphosis of the blood, it is as difficult as it is hazardous to attempt to explain the various causes upon which the differences between venous and arterial blood are founded. There are, as I shall proceed to show, decided differences between the blood of the renal arteries and veins, and between the blood of the hepatic vein and of the vena portæ; and yet, as has been already shown, the differences between the blood of the aorta and of the vena cava are very immaterial and trifling. To produce this ultimate similarity, other changes (not yet heeded by the physiologist) must have largely contributed.

*Properties of the blood of the vena portæ ;—its comparison  
with arterial blood.*

The blood of the vena portæ in horses (the only animals in which I have examined it) is darker than ordinary venous blood; the difference of the tint is however so slight, as to be observable only upon actual comparison. It coagulates more slowly than ordinary arterial or venous blood; the clot is less firm, more of a gelatinous appearance, and falls to pieces if an attempt be made to lift it. I analysed the blood of the vena portæ of the two horses already alluded to. If arterial, ordinary venous, and vena portæ blood are deprived of their fibrin



by whipping, and are then allowed to stand, the blood-corpuscles subside in nearly equal times; but while they occupy little more than one half of the volume of arterial or ordinary venous blood, in portal blood they form nearly three fourths of the whole volume.

In portal blood, after the lapse of several hours, a delicate glittering film was formed upon the surface of the serum, which when seen under the microscope was found to contain fat-globules; I could not however discover any lymph-granules either in the serum or amongst the blood-corpuscles. The arterial and ordinary venous blood, on the contrary, exhibited lymph-granules, but no fat-globules.

The blood of the vena portæ not only contains less fibrin than arterial or ordinary venous blood, but the qualities of that constituent are also different; it is not so consistent as ordinary fibrin, and does not separate into the firm, globular, little masses that are obtained by whipping arterial blood.

Our knowledge of the properties of this blood has been materially increased by the researches of Schultz.<sup>1</sup> The following are his principal conclusions: It is darker than ordinary venous blood, but the difference of tint is sometimes so slight, as to be hardly perceptible. It is darkest in fasting horses, but after a full meal, it becomes brighter. These differences are more striking than those between arterial and venous blood. Common salt, nitre, atmospheric air, and even oxygen, when shaken with the dark blood of the vena portæ, have scarcely any effect upon the colour, whereas venous blood would be changed to a brighter red by these reagents. If the blood of the vena portæ be not extremely dark, a slight change is perceptible.

If a portion of this black blood be treated with a quantity of common salt or nitre sufficient to prevent it from coagulating, coagulation may still be induced (although not until after several hours, and then very slightly) by the addition of water, while venous blood similarly treated coagulates in the course of five or ten minutes.

If the blood is very dark, it sometimes does not coagulate at all; if it is not very dark, it occasionally coagulates in the same time as ordinary venous blood; the clot, however, is very

<sup>1</sup> System der Circulation, p. 140.

soft, and either entirely, or at least its lower surface, dissolves in the course of from twelve to twenty-four hours. Schultz further observes that after the blood has been whipt, the corpuscles sink very quickly; he ascribes this peculiarity to an excess of colouring matter attached to the capsules of the blood-corpuscles.

As the blood of the vena portæ that I analysed was taken from the same two horses from which I obtained the arterial and venous blood, a fair comparison may be instituted with respect to their differences of constitution.

1000 parts contained :

	Analysis 1. Arterial blood.	Analysis 5. Blood of vena portæ.
Water . . . .	760·084	724·972
Solid residue . . . .	239·952	257·028
Fibrin . . . .	11·200	8·370
Fat . . . .	1·856	3·186
Albumen . . . .	78·880	92·400
Globulin . . . .	136·148	152·592
Hæmatin . . . .	4·827	6·600
Extractive matter and salts	6·960	11·880
100 parts of blood-corpuscles contained 3·4 of hæmatin.		100 parts of blood-corpuscles contained 4·1 of hæmatin.

	Analysis 3. Arterial blood.	Analysis 6. Blood of vena portæ.
Water . . . .	789·390	815·000
Solid residue . . . .	210·610	185·000
Fibrin . . . .	6·050	3·285
Fat . . . .	1·320	1·845
Albumen . . . .	113·100	92·250
Globulin . . . .	76·400	72·690
Hæmatin . . . .	3·640	3·900
Extractive matter and salts	10·000	11·632
100 parts of blood-corpuscles contained 4·7 of hæmatin.		100 parts of blood-corpuscles contained 5·3 of hæmatin.

It is only in four respects that the results obtained by a comparison of these two analyses of the blood of the vena portæ with arterial blood at all coincide: the former contains less fibrin, more fat, more extractive matter and salts than the latter, and lastly, the proportion of colouring matter to globulin is greater in the former.

In order to give a better idea of the relative proportions of the colouring matter, I shall quote another analysis of the

blood of the vena portæ, which was made for the purpose of comparison with the blood of the hepatic vein.

In this analysis the colouring matter is separated into hæmatin and hæmaphæin. I obtained from 1000 parts :

Analysis 7.					
Water . . . . .	.	.	.	.	801·500
Solid residue . . . . .	.	.	.	.	198·500
Fibrin . . . . .	.	.	.	.	6·200
Fat . . . . .	.	.	.	.	2·700
Albumen . . . . .	.	.	.	.	90·000
Globulin . . . . .	.	.	.	.	75·600
Hæmatin . . . . .	.	.	.	.	3·400
Hæmaphæin . . . . .	.	.	.	.	1·800
Extractive matter, with some hæmaphæin, } and with salts . . . . . }					14·400

This blood was very rich in colouring matter, there being no less a proportion of it than 6·8 in 100 parts of blood-corpuscles, of which 4·5 were hæmatin and the remaining 2·3 hæmaphæin. In addition to this, the extractive matters retained a considerable quantity of hæmaphæin.

The circumstance that the blood of the vena portæ in analysis 6 contains less solid residue, and a smaller proportion both of albumen and blood-corpuscles than arterial blood, while the reverse is observed in analysis 5, need not excite much surprise when we remember that in analyses 3, 4, and 6 the blood was taken from an old, decrepid, starved animal.

Schultz<sup>1</sup> has made some very important observations on the relative constitution of the blood of the vena portæ, as contrasted with arterial and ordinary venous blood.

#### *Solid constituents.*

The blood taken from the vena portæ of fasting horses gave, as a mean of three analyses, 16·90% of solid constituents, while arterial and venous blood gave 15·56% and 18·6% respectively :

<sup>1</sup> Schultz's analyses of the portal blood would, in my opinion, have yielded more important results, both as regards the absolute and the comparative composition of the fluid, if he had determined all the constituents from the same identical blood. He appears to have used the blood of different animals for the determination of the different constituents. The absolute composition of the blood is assuredly different in different animals, but there are also relative differences depending on age, nutrition, and other circumstances.

it contained therefore (in this instance) a greater proportion of solid constituents than arterial; a less proportion than venous blood. This proportion, 16·90%, is however less than is usually met with in arterial or venous blood.

The blood of the vena portæ of a horse fed with oats gave 20·3% of solid constituents, while the arterial and venous blood of the same animal gave 22·91% and 19·5% respectively. Here the solid constituents of the blood of the vena portæ bear an exactly opposite proportion to those of arterial and venous blood, for in this case they exceed those of arterial, and are less than those of venous blood.

The amount of the per-centage of the solid residue, although still deficient, approximates very nearly to the ordinary average.

My observations from analysis 5 are at variance with these remarks.

#### *Fibrin.*

As an average of three analyses, 3·2% of fibrin was obtained from the blood of the vena portæ, while the proportions obtained from arterial and venous blood were 1·04% and 1·09% respectively. Hence it may be concluded that this blood is poorer in fibrin than either arterial or venous blood—a point which is confirmed by my own observations.

#### *Albumen with salts, and blood-corpuscles.<sup>1</sup>*

The following results were obtained from his analyses :

	1.	2.	1.	2.	1.	2.
	Blood of vena portæ.		Arterial blood.		Venous blood.	
Albumen . . .	8·16%	9·67%	9·86%	11·11%	7·96%	11·25%
Blood-corpuscles . .	8·74%	10·53%	4·65%	10·21%	9·21%	6·95%

The analyses 1 were made with the blood of fasting horses; the analyses 2 with the blood of horses after a recent meal of oats. Hence it follows that the blood of the vena portæ contains more blood-corpuscles and less albumen than arterial or venous blood. My own analyses do not exactly coincide with these remarks.

#### *Fat.*

The solid residue of the blood of the vena portæ gave (as the mean of four analyses) 1·66% of fat, while the corresponding

<sup>1</sup> Schultz's method of analysis is described in note 1, p. 198.



proportions of fat in arterial and venous blood amounted to only  $\cdot 92\%$  and  $\cdot 83\%$  respectively. Hence it appears (and in this respect my own observations confirm those of Schultz) that this blood contains a larger proportion of fat than either arterial or venous blood. The albumen and the clot contain individually a larger quantity of fat in this than in ordinary blood. Schultz has observed a very striking difference between the quantity of fat contained in the fibrin of this and of arterial blood: the former yielded  $10\cdot 7\%$ , while the latter gave only  $2\cdot 34\%$  of fat, which in the first case was brown and discoloured, in the latter was white and crystalline.

It follows from these remarks that there is no constancy in the deviations of the blood of the vena portæ from arterial or venous blood. The reason of the mutability of the composition of this blood is easily accounted for, if we consider the relation that the ramifications of the vena portæ bear to the digestive organs, and the absorbent power of the veins, as shown by the experiments of Magendie,<sup>1</sup> Tiedemann, and Gmelin.<sup>2</sup>

The rapid removal of water from the stomach can, moreover, only be explained by the agency of the vena portæ.

Hence it is evident, both from my own analyses and those of Schultz, that the blood which is conveyed to the liver by the vena portæ differs in well-fed and in fasting animals.

When fluids, containing a smaller proportion of solid residue than ordinary blood, are absorbed by well-fed animals, we may naturally infer that the blood of the vena portæ will be more deficient in solid constituents than either arterial or venous blood. This view is confirmed by the observations of Schultz, excepting in the case of the horse that had been fed with oats shortly before its death, when a greater solid residue was left by this blood than by either the arterial or venous: in this instance, however, the residue was below the ordinary average of either venous or arterial blood. In fasting horses the residue is considerably below the average of ordinary blood.

The remarkably small quantity of fibrin that is invariably found in the blood of the vena portæ, as well as the large proportion of fat that is associated with the fibrin, is a point of considerable interest; as also the large proportion of blood-corpuscles

<sup>1</sup> Précis élémentaire de Physiologie, par Magendie. Bruxelles, 1838, p. 328.

<sup>2</sup> Müller's Physiologie des Menschen, vol. 1, p. 241.

observed by Schultz, and which occurred, in rather a striking degree, in my analysis 5.

It is of importance to trace the origin and development of these peculiarities, as we may thus be led to take clearer views of the functions of the liver and the preparation of the bile.

Schultz<sup>1</sup> attributes the source of all these peculiarities to the intestinal canal, to the lymphatic glands, and to the spleen.

The organization and vitality of the chyle, prepared in the intestinal canal, require (according to Schultz,) the co-operation of the plasma, which (being thus partially consumed) leaves a large proportion of blood-corpuscles, the majority of which appear to have been deprived of their nuclei by absorption, and to have been converted into empty capsules impregnated with colouring matter. To this is attributable the preponderance of the clot. The large quantity of fat is ascribed by Schultz to absorption of the chyle, and he considers that its dark colour is in some way connected with the metamorphosis of the colouring matter of the blood-corpuscles.

My own views with respect to the causes of the peculiar constitution of this species of blood differ, in a few immaterial points, from the ingenious explanation of Schultz.

There are two reasons for the very small quantity of fibrin in this blood. In the first place it may take up a quantity of fluid containing little or no fibrin, by which means the relative proportion of fibrin in a given quantity of blood must of course be diminished; and, secondly, it may be explained by the torpid motion in this part of the circulatory apparatus, and the deficiency of atmospheric oxygen: this latter reason may also account for some of its other peculiarities. In consequence of the deficiency of oxygen, the metamorphosis of the blood-corpuscles must be imperfect, deficient, and retarded, and the solution of the developed corpuscles will not be duly effected. To this cause we must ascribe not merely the diminished quantity of fibrin, but the retarded solution, and the accumulation of the corpuscles, especially of such as are fully developed and abound in hæmaphæin, the consequent accumulation of that colouring substance in the plasma, and the necessarily dark tint of the serum, which possesses no means of throwing off that constituent.

<sup>1</sup> Op. cit. p. 322.

The large proportion of fat is chiefly attributable to the fluids that are produced during the act of digestion, and which are conveyed into the portal vein. In examining this blood under the microscope, I have seen that it is rich in fat globules. The deep yellow (or sometimes even brown) tinge of the fat is produced by hæmaphæin, which is very soluble in fat and cannot easily be extracted from it.

The fatty acids do not seem to undergo any change in the liver, for we find them, as well as the cholesterin of the blood, again in the bile. The cholesterin is particularly abundant, and is probably one of the products of the function of the liver.

*Properties of the blood of the hepatic vein;—its comparison with the blood of the vena portæ.*

I am not aware of any analyses of the blood of the hepatic vein having been made previously to my own.

Very important conclusions might doubtless be drawn respecting the constitution of the bile, by contrasting the analyses of the blood of the vena portæ with that of the hepatic vein, if it were not that we had to take into consideration with the former the blood of the hepatic artery with which it mixes in the capillary system of the liver.

As the contents of the hepatic vein are discharged into the vena cava inferior, immediately as it leaves the organ, it is no easy matter to obtain any considerable quantity of the blood in a pure and unmixed state.

Professor Gurlt has kindly assisted me in collecting specimens of this blood from horses.

The blood of the hepatic vein differs, in several respects, from any of the forms of blood that have been hitherto considered.

It appears to be darker than the blood of the vena portæ, (when contrasted with it,) but becomes of a somewhat brighter colour by continued stirring.

The separation of the fibrin is more difficult and tedious than from the blood of the vena portæ, and this constituent, when deposited on the rod, is possessed of very little consistence, is soft, gelatinous, and difficult to wash, a portion of it falling to pieces and being distributed through the water. The blood, after the removal of the fibrin by whipping, continues to manifest a tendency to gelatinize; the blood-corpuscles de-

posit themselves and form a dark coagulated clotted mass under the surface of the serum, from which no additional fibrin can be obtained by further stirring; and upon allowing it to rest, the same phenomena are again exhibited. On placing a little of the blood, immediately after stirring, on a glass slip, the blood-corpuscles may be seen to collect into minute islets or spots; at least I observed this to occur in three specimens of this sort of blood that I analysed at different times.

In one instance I found that the blood had actually coagulated, but slowly, after the removal of fibrin by whipping, and upon renewed stirring I obtained a small quantity of stringy or coriaceous fibrin.

*Microscopic analysis.* On examining a specimen of this blood, not diluted with the ordinary solution of salt, the swollen corpuscles were observed moving about; some were distinct, some partially united with others; these gradually attached themselves to one another and formed irregular groups of various sizes, in which the outlines of the individual corpuscles could no longer be recognized. It appeared as if the corpuscles exuded a plastic matter, which might possibly be the cause of their adhering to each other.

On diluting the blood with a solution of hydrochlorate of ammonia, I once observed that the medium-sized corpuscles appeared studded with minute pearly beads, (vide supra, page 105.) The following observation which I made upon two occasions interested me extremely. I saw a great excess of small blood-corpuscles, about one fourth or one sixth of the ordinary size, whose true nature could only be recognized by their well-marked yellow colour, and by their passing from a spherical into a flattened form, when rotation was excited. The motions of these minute blood-corpuscles resembled those of Brown's molecules, and were much more active than those of the ordinary corpuscles in common blood.

The analysis of the blood of the hepatic vein gave in 1000 parts—



	Analysis 6. Blood of vena portæ.	Analysis 8. Blood of hepatic vein.
Water . . . .	815.000	814.000
Solid residue . . . .	185.000	186.000
Fibrin . . . .	3.285	2.650
Fat . . . .	1.845	1.408
Albumen . . . .	92.250	103.283
Globulin . . . .	72.690	57.134
Hæmatin . . . .	3.900	3.000
Extractive matters and salts	11.623	12.312
	100 parts of blood-corpuscles contained 5.3 of hæmatin.	100 parts of blood-corpuscles contained 5.2 of hæmatin.

The blood was taken from the starved horse, who supplied the matter for analyses 3 and 4.

	Analysis 9. Blood of vena portæ.	Analysis 10. Blood of hepatic vein.
Water . . . .	738.000	725.000
Solid residue . . . .	262.000	275.000
Fibrin . . . .	3.500	2.500
Fat . . . .	1.968	1.560
Albumen . . . .	114.636	130.000
Globulin . . . .	116.358	112.000
Hæmatin . . . .	4.920	4.420
Hæmaphæin . . . .	1.467	1.040
Extractive matters and salts	16.236	17.160
	100 parts of blood-corpuscles contained 5.4 of colouring matter, of which 4.2 were hæmatin and 1.2 hæma- phæin.	100 parts of blood-corpuscles contained 4.8 of colouring matter, of which 3.9 were hæmatin and 0.9 hæma- phæin.

From these analyses we deduce the following conclusions. The blood of the hepatic vein is richer in solid constituents than that of the vena portæ, and consequently than either arterial or ordinary venous blood; it contains less fibrin, fat, globulin, and colouring matter, than the blood of the vena portæ; the ratio of the colouring matter to the globulin is smaller, and the quantity of albumen larger in the former than in the latter form of blood.

In consequence of the admixture of the blood of the hepatic artery with that of the vena portæ in the capillary system surrounding the biliary ducts, and of the catalytic influence of the cells of the liver in the formation and secretion of bile, it is impossible for us to ascertain the relative parts which these two distinct forms of blood play in the production of this important

secretion, or to state with certainty which constituents are drawn from the contents of the hepatic artery and which from those of the vena portæ, or how the withdrawal of them is effected.

These analyses are nevertheless of great importance, since they show that the blood-corpuscles are actively engaged in the secretion of the bile, a view which corresponds with and tends to explain other phenomena connected with this secretion. They show that the blood of the hepatic vein contains more albumen and less globulin, or (which is much the same thing) blood-corpuscles, than that of the vena portæ. These differences favour the hypothesis that the corpuscles (or, at least, their principal constituent, the globulin,) have a greater share in the formation of the bile in the peripheral system of the liver than the albumen, the principal constituent of the plasma.

Another corroborative circumstance is the small amount of colouring matter in the blood of the hepatic vein, from which we infer that some of it has been consumed in the formation of the bile, a view which accounts, with more probability, for the origin of its colour than the supposition that it is produced from a portion of the plasma.<sup>1</sup>

If the liver were supplied with blood from the vena portæ alone, there could be hardly a doubt entertained with regard to the correctness of my hypothesis; the influence of the blood of the hepatic artery must not, however, be overlooked. If, for instance, the blood of the hepatic artery contained a much larger proportion of albumen and a smaller quantity of blood-corpuscles than the blood of the vena portæ, the mixture of these would produce a fluid similar in constitution to the blood of the hepatic vein. But, upon comparing the blood of the vena portæ with that of the hepatic artery, no such proportions, as those we have assumed, are observable. It is true that a mixture of the two bloods in a badly fed animal would contain more albumen, but, at the same time, more blood-corpuscles than the blood of the vena portæ (see Analyses 3 and 6); and in the reverse case (see Analyses 1 and 5) the mixture would

<sup>1</sup> [This view is corroborated by Mulder, who observes that if the blood-corpuscles undergo a metamorphic change prior to their development into living tissue, the products of the decomposition of the hæmatin may be probably traced in the *bili-fulvin* of the bile. (Versuch einer allgemeinen physiologischen Chemie, p. 358.)]

contain fewer corpuscles, but, at the same time, less albumen, than the blood of the vena portæ.

It is impossible to account for so large an amount of albumen in the blood of the hepatic vein, if we consider the quantity of bile which is secreted by the healthy liver, and attribute its formation to the elements of the plasma alone ; whereas, if we consider the bile to be formed at the expense of the blood-corpuscles, the peculiarities in the blood of the hepatic vein are at once accounted for.

In addition to the separation of the bile, the liver effects a further change in the blood by drawing from that fluid the sources of its own nutrition. These two processes merge into one, which may be regarded as the product of the development of the hepatic cells. The formation and secretion of such a complicated fluid as the bile, by the action of the hepatic cells on the plasma, may be dependent on various causes. The entire structure of an organ must necessarily correspond with its functions, and with every variety of internal organization there will be a corresponding variation in the secretion. The action of the hepatic cells on the plasma is different from that of the renal or other glandular cells, in consequence of the difference of their chemical action on the blood. The nerves also seem to influence the secretions.

Further, since the plasma has been modified in its progress through the liver by the solution of a large number of blood-corpuscles, a corresponding new product must be evolved from it by the hepatic cells. I have previously stated that the development, and especially the ultimate solution of the blood-corpuscles may occur in all parts of the peripheral system, if a sufficient supply of oxygen be present. I have shown that a large quantity of fully developed corpuscles accumulates in the blood of the vena portæ, in consequence of its torpid motion and the want of a due supply of oxygen ; if this blood mixes in the capillaries with the well-oxygenised blood of the hepatic artery, it is not difficult to conceive that a proportionably larger quantity of blood-corpuscles is thus dissolved in a given time than at many other parts of the peripheral system, that the plasma may thus become changed, and that the product of the general action of the hepatic cells may be different.

It is well known that the liver is one of the most active

organs of the animal economy. Even in the embryo, the development of its cells is wonderfully abundant, as has been shown by Reichert. In the adult the activity of the liver is exhibited by the increased secretion of the bile during digestion. The activity of an organ is represented by the integral of the activity of its cells; and the increased activity of the cells is intimately connected with the facility of evolution and revolution. If, then, in consequence of the activity of the liver as a secreting organ, a large number of cells are consumed, it follows that a proportionably large number must be reproduced; and we can thus explain the apparently inconsistent phenomena of the blood of the hepatic vein containing less fibrin than that of the vena portæ, by the supposition that, although a large quantity of blood-corpuscles is consumed by the liver, the fibrin of the plasma supplies the materials for the formation of cytoblasts for new cells.

All the other differences that are observable between the composition of the blood of the hepatic vein and of the vena portæ may be accounted for by paying a little attention to the nature of the bile.

The bile contains a smaller proportion of solid constituents than the blood; hence it is obvious that the blood, previously to the separation of the bile (*i. e.* the blood of the vena portæ) must contain a smaller proportion of solid constituents than after this change has been effected (*i. e.* the blood of the hepatic vein.)

The blood of the vena portæ contains more colouring matter, both hæmatin and hæmaphæin, than that of the hepatic vein. It is impossible to decide with certainty upon the manner in which these colouring substances are consumed in the liver, as we are still deficient in correct ultimate analyses of biliphæin and hæmaphæin; we may, however, safely conclude that the biliphæin is produced by the metamorphosis of the colouring matter of the blood.

*Properties of the blood of the renal veins;—its comparison with the blood of the aorta.*

The blood of the renal veins was drawn from a horse simultaneously with the aortic blood; it was found, however, upon opening the body of the horse, bled to death, that the renal



veins contained so small a quantity of blood that Professor Gurlt was unable to collect from them more than about 50 grains.

The blood obtained in this manner was visibly darker than the aortic blood. I stirred it for a considerable time with a rod, but could obtain no fibrin; on leaving it to stand, it became gelatinous, and resembled the blood of the hepatic vein after similar treatment.

*Microscopic analysis.* Upon comparing the two sorts of blood under the microscope, the only perceptible differences were the following: In the unmixed blood of the renal veins the corpuscles united themselves into islets and amorphous groups, in which the individual globules could not be traced. Upon mixing some of this blood with a solution of salt, a larger quantity of small and middle-sized corpuscles were observed than in the aortic blood when similarly treated. The proportion, however, of the small corpuscles to the large ones was not so striking as in the blood of the hepatic vein. (Vide supra, p. 209.)

In consequence of the small quantity of material, I resolved to determine only the most important of the constituents. I made an accurate estimate of the proportions of water and albumen, but was prevented by illness from ascertaining the quantities of globulin and hæmatin.

1000 parts of blood contained:

	Analysis 11. Aortic blood.	Analysis 12. Blood of renal vein.
Water . . . .	790·000	778·000
Solid residue . . .	210·000	222·000
Fibrin . . . .	8·200	?
Albumen . . . .	90·300	99·230

From these analyses it appears that the blood of the renal veins is more abundant in solid constituents and in albumen than the aortic blood, but that it contains less fibrin and fewer blood-corpuscles.

The two latter inferences, respecting the quantity of fibrin and of blood-corpuscles in the blood of the renal vein, cannot be drawn from the analyses in the same certain manner as in the comparative analyses of the blood of the hepatic vein and of the vena portæ.

Although I cannot believe that this blood is entirely devoid of separable fibrin, it certainly contains less fibrin than arterial blood. In fact it is more than probable that the quantity of fibrin which is formed during the course of the blood through the renal capillary system, where oxygen is taken up and not again supplied, does not exceed the quantity consumed. Although no determination of the hæmatin and globulin was instituted, we may infer, analogically, from our former analyses, and from the necessary reciprocating proportions of the two principal constituents of the blood, that less hæmatoglobulin exists in the blood of the renal veins than in that of the aorta. If the albumen in each be estimated in regard to equal quantities of the solid residue, the albumen in the aortic blood will be found to be to that in the blood of the renal vein in the ratio of 4.25 to 4.46. The quantities of hæmatoglobulin will therefore be in an opposite ratio.

These results throw considerable light upon the changes which the blood undergoes in the kidneys. It loses a certain quantity of water, which is accounted for by the urine. Hence this blood contains less water than the aortic blood.

Urea appears to be formed from the corpuscles, under the cooperating influence of the plasma and oxygen of the blood, rather than from the albumen, which preponderates in the blood of the renal veins the same as in the hepatic vein. It cannot be *positively asserted* that the observations which were made regarding the trifling amount of fibrin in the blood of the hepatic vein, as compared with that in the blood of the vena portæ, here hold good, but there are many reasons in favour of such an analogous view.

It is highly probable that the activity of the excreting powers of the kidney is due to the activity of the organ itself, as has been already observed with regard to the liver, and that this activity corresponds with the energetic evolution and revolution of renal cells.

That the kidneys do not separate bile, but urea, uric acid, and salts, is due partly to the chemical constitution of the renal cells and to the peculiarly directed cooperation of the nerves of these organs, and partly, perhaps, to the composition of the blood itself, which differs from that which supplies the liver.

The separation of the water is caused by the peculiar internal

structure of the organ ; it cannot be regarded as a product of the development of the cells, or of the metabolic power of the cells acting on the plasma ; but the water is separated in much the same manner as the various gases of the blood are removed by the lungs.

But whether the salts which are separated by the kidneys, the combinations of chlorine, and of phosphoric, sulphuric and lactic acids, are, so to speak, mechanically carried away in the water in which they are held in solution, and which permeates the textures of the kidney, or whether their separation is to be regarded as a true secretion of the renal cells, due to their organised development, is a point which I have no means of ascertaining. An accurate analysis of the kidneys would soon show whether the salts which have been mentioned do or do not belong to the constitution of the renal cells, a point which the analysis of Berzelius has left undecided. These salts, most of which preexist in the blood, at all events find their way into the renal cells, and either are or are not connected with their peculiar vital development. The former is far the more probable ; and in that case the secretion of the salts would not be a mere mechanical act, but would be due to organic causes.

The kidneys separate hæmaphæin from the colouring matter produced by the metamorphosis of the blood-corpuscles, and the proportion in which they separate it is larger than the proportion contained in the plasma, a circumstance which is obvious from the colour of the urine being generally deeper than that of the liquor sanguinis. Hence it is very probable that a portion of the colouring matter is formed by the metamorphosis of the corpuscles in the peripheral system of the kidney. The kidneys likewise separate another colouring matter, uroerythrin ; in a normal state, only in a slight proportion, but in certain pathological conditions, in a comparatively large quantity. Uroerythrin, in all probability, owes its origin to the hæmatin of the blood-corpuscles. As the proportions of uric acid and of uroerythrin to urea are very small in normal urine, but are much increased in certain pathological conditions, we must infer that, in these latter cases, the blood undergoes some peculiar change.

*Comparison of the venous blood with the blood of the capillaries.*

It is well known that blood taken from the body by scarification does not materially differ in its physical properties from venous blood ; it takes about an equal time to coagulate, and separates into clot and serum. The blood which flows from leech-bites is also similar to venous blood. From comparative analyses of venous blood and blood taken by leeches or cupping, Dr. Pallas<sup>1</sup> concludes that the (so termed) capillary blood is richer in solid and coagulable constituents than either venous or arterial blood.

The ratios are represented by the following numbers :

$$2.550 : 3.100 \quad \text{and}$$

$$2.550 : 2.630$$

Denis<sup>2</sup> contradicts these statements ; he observes that the blood of the capillaries, when taken by cupping, is of a bright red colour and very plastic if it is taken from the neighbourhood of a large artery, but that it is dark and proportionally less plastic when drawn from the vicinity of large venous trunks ; so that its characters always present a certain degree of similarity to either arterial or venous blood. Denis analysed blood drawn from the arm of a man aged 70, and blood taken by cupping from the left side of the thorax of the same individual, and compared the results. 1000 parts contained :

	Blood from the arm.	Blood obtained by cupping.
Water . . . .	790.0	790.0
Fibrin . . . .	2.7	2.9
Albumen . . . .	56.0	54.0
Hæmatin . . . .	131.6	133.4
Oxide of iron . . . .	0.7	0.7
Phosphorized fat . . . .	8.0	8.2
Cruorin . . . .	1.1	1.0
Carbonate of soda . . . .	1.0	1.0
Chloride of sodium . . . .	4.0	4.0
Chloride of potassium . . . .	2.1	2.0
Carbonate of lime . . . .	1.3	1.3
Phosphates of lime and magnesia . . . .	0.5	0.5

Or,

Water . . . .	790.0	790.0
Blood-corpuscles . . . .	132.3	134.1
Solid residue of serum . . . .	77.7	75.9

<sup>1</sup> Journal de Chimie Médicale, Oct. 1828.

<sup>2</sup> Recherches, p. 72.



Denis also analysed the blood of a girl, aged 27, in a similar manner, and obtained corresponding results from both forms of blood. (*Recherches*, pp. 152, 153, and 250.)

REVIEW OF THE MODIFICATIONS AND CHANGES THAT THE BLOOD UNDERGOES IN THE COURSE OF THE CIRCULATION.

Having in the previous section given my views respecting the probable changes that the blood undergoes in the course of the circulation, founded partly on numerous analyses of that fluid, and partly on conclusions deduced from the necessary connexion that exists between the phenomena of secretion and of metamorphosis; and having also endeavoured to explain the variations that occur in the blood of the same individual, through the influence of nutrition and the secreting organs (as the liver and kidneys), I beg once more to call the attention of the reader to the subject under consideration.

My views regarding the formation of the products of secretion from the changes that the blood undergoes in the organism require a more searching investigation before confidence can be placed in them. There is nothing improbable in the supposition that the blood is changed in the manner that I have assumed; I can as easily conceive that the urea and bilin are formed by the mutual action of the blood-corpuscles and the liquor sanguinis, as that their origin is dependent upon the liquor sanguinis alone; but for reasons already communicated, there is a greater degree of probability in the idea that these substances are produced by the metamorphosis of the blood-corpuscles. These reasons are founded more on the intimate connexion that exists between the products of secretion, change of matter and blood, and on the mutual adaptation and principle of compensation in the organism of the animal body, than on the physical and chemical "momentum" of the circulation and of secretion; and the question we have now to consider is, whether in the latter there is not something directly opposed to our views respecting the metamorphosis of the blood.

Before proceeding to these investigations, I must in the first place revert to some of the points connected with this metamorphic action.

The first and principal object of the blood is the nutrition

of the organism, and for this purpose the circulating fluid is modified and consumed in the peripheral system. We have conjectured that the extractive matters of the blood which are removed by the kidneys are thus formed. The constant modification and consumption of blood dependent on the act of nutrition render the supply of fresh nutrient fluid, and the removal of effete matter, indispensably necessary, since a proper constitution of the blood is requisite for the due performance of the function of nutrition. The effete matters are replaced by chyle mixed with lymph; and this fluid must of necessity be converted into blood, as otherwise the blood would soon consist entirely of chyle. The change is effected by the formation of young blood-corpuscles, (an act which is accompanied by the consumption of chyle-, lymph-, and oil-corpuscles,) and by the fibrin of the chyle becoming more plastic; all the other fluid constituents of the chyle are similar to those of the liquor sanguinis, except that there is an excess of water and of extractive matters in the former. If therefore we suppose a continuous formation of blood-corpuscles, the necessity for their consumption must be sufficiently obvious. I have assumed that fibrin is formed as a consequence of this consumption, and that this newly-formed fibrin supplies the place of that which is employed for the purposes of nutrition in the peripheral vascular system. I have also shown, (page 163,) that there is no difficulty in the idea of the formation of albumen; and lastly, I attempted to show that, in all probability, urea, uric acid, and bilin are formed as a consequence of this consumption of the blood-corpuscles. For these substances must necessarily be formed as products of the changes which the constituents of the blood undergo in the circulation, and are not (as observations on starved and emaciated individuals show us) a consequence of the changes which the circulating fluid undergoes during the nutrition of the tissues, but are dependent on the metamorphic action that is produced by the respiratory process. It is principally the blood-corpuscles, (as I have endeavoured to show, in page 155,) that are connected with the consumption of oxygen; and when we reflect that this change in the corpuscles must take place under similar conditions in animals both high and low in the scale of development, we can understand how it is that urea, uric acid, and bilin occur in the renal and hepatic

secretions of animals of nearly every form of structure, and under such varying phases of existence.

I will now proceed *seriatim* with the objections that may be urged against my views respecting the metamorphosis of the blood.

Analyses of the urine show us that it contains a greater amount of urea and uric acid than of extractive matters; assuming that the former substances, and the bilin, are products of the metamorphosis of the blood-corpuscles, and that the latter are the products of the change that the plasma undergoes in the nutrition of the peripheral system, the mass of the former is greater than the mass of the latter. If, moreover, a portion of the extractive matter is in reality not removed by the kidneys, but is, as I have already suggested, in page 150, again adapted in the circulation to the purposes of nutrition, (serving probably for the cytoblastema of the cells of the cartilaginous and gelatinous tissues), then the separation of so considerable a quantity of the product of the metamorphosis of the blood-corpuscles ought still to surprise us, if its only purpose were to supply the fibrin, and possibly a part of the consumed albumen in the plasma.

It can, however, be easily shown that another and a much more important final result must be considered in the consumption of the blood-corpuscles. For if, as I have shown, in page 155, the blood-corpuscles are principally concerned in the consumption of the atmospheric oxygen, then it is clear that the greater part of the carbon, which is exhaled from the lungs as carbonic acid, must originate from them, and the source of animal heat would thus be chiefly attributable to the metamorphosis of the blood-corpuscles. Consequently, the chemical modifications of the blood-corpuscles are of at least as much importance as the act of nutrition in the peripheral system carried on by the agency of the plasma, inasmuch as they are subservient to the most essential and indispensable requisite for animal life. The other purposes of the corpuscles appear also to be subservient to this great end.

If the blood-corpuscles (from the period of their development up to their final solution) convert as large a quantity of carbon as is generally assumed, into carbonic acid, in order to maintain a proper degree of temperature, then we cannot be astonished at the amount of the products of secretion of the



kidneys and liver, which we have assumed to be consequent on the metamorphosis of the blood-corpuscles ; for since the animal matters undergo a chemical change by the elimination of the carbon, the products which are then formed must be removed, in order that the blood may retain its normal composition.

In opposition to the assertion that the urea, uric acid, and bilin are products of the metamorphosis of the blood-corpuscles, it may be urged that the daily amount of these secretions involves a larger daily consumption of blood-corpuscles than appears to be consistent with the rate of their reproduction, as far at least as our knowledge of the act of formation of the corpuscles would lead us to infer.

I have mentioned, in page 155, that the blood-corpuscles are to be regarded as cells, whose development must be considered as perfectly analogous with the development of other cells. In absorbing from the plasma the substances requisite for their nutrition, and in rejecting the products that must be consequent upon the act of absorption, they obviously exert a modifying influence on that fluid. The blood-corpuscles do not, however, find their way into the circulating fluid in a matured form, but their cytoblasts enter it as germs of the future corpuscles, and require the assistance of the atmospheric oxygen to attain their perfect development. The only hypothesis we can frame regarding the primary formation of the blood-corpuscles is, that they are produced from the plasma, that their entire development and increase of bulk is due to the reciprocal action of the young blood-corpuscular cells and plasma on each other at the expense of the latter, and that up to the moment when the blood-corpuscles cease to discharge their functions as independent organisms in the circulation, every change that occurs in them must be accompanied by a simultaneous alteration in their cytoblastema, the plasma.

It may further be urged that, in order to account for the formation and secretion of urea, uric acid, and bilin, there is no necessity for the assumption that there is a metamorphosis of the blood-corpuscles. These substances might as easily have been formed in the process of chylification, or during the conversion of the chyle into blood, or from the albumen, instead of from the corpuscles.

I have already mentioned that it is by no means probable that these products of secretion are formed in the act of nutri-



tion, since they are produced in fasting persons, and even when nearly all the soft tissues are wasted away.

We do not, however, intend to assert that nutrition exercises no influence over these products, or that the peculiar structure of each secreting organ is not to be considered. Nevertheless I cannot agree with certain physiologists who maintain that in granivorous animals, sugar formed in the chyle is the cause of the carbonic acid evolved from the lungs, or that urea, uric acid, and bilin are formed solely from the albumen, and that the blood-corpuscles take no part in this action; for the uniform and simultaneous formation of carbonic acid, urea, uric acid and bilin, in animals whose food is so varied, and whose habits and conditions of life are so diversified, renders it probable that these substances are simultaneously formed, as a consequence of one and the same metamorphic act. On the other hand, we must not omit to notice that the occurrence of the non-nitrogenous hippuric acid in the ruminantia, the excessive production of uric acid accompanied frequently with a total absence of urea in birds and amphibia, and the inverse ratio in which these substances occur in man, monkeys, &c., as likewise the different chemical relations of the bile in fishes and amphibia, point out the influence of nutrition and of the organization in general on these secretions. What is the ultimate purpose of the blood-corpuscles in the organism if they do not participate in the formation of these products, and if they experience no real material change? The idea that the nutrition of the tissues is accomplished by the aggregation of blood-corpuscles is now abandoned, and the supposition that these molecules exert a vitalizing influence on the organized tissues is perfectly unintelligible. I can form no conception of a blood-corpuscle that is not undergoing a continuous material change, and I regard this change as the ultimate object of its existence.

Daily experience shows us that the fluids which are secreted by the principal glands take their origin from the blood: the question then arises whether these secretions exist in the blood itself, that is to say, whether the blood which enters a secreting organ, as the kidney or liver, indicates a difference of composition as it leaves that organ. At first sight we should doubtless answer this question in the affirmative; but taking into

consideration the rapidity of the circulation, and the short space of time in which the same blood is supposed to remain in an organ, it is obvious that the detection of the changes in the blood, due to the removal of the secretions, will be a task, if not absolutely impossible, at least extremely difficult.

The question whether the blood of the same individual possesses any traceable differences, is most intimately connected with the physico-chemical "momentum" of the circulation; although sufficient facts and experiments are still wanting to enable the point to be decisively settled, I believe from an estimate of all that is at present known on the subject, that we are warranted in the assumption that there does exist a difference in the blood of one and the same individual.

According to Hering's experiments,<sup>1</sup> (in which he injected ferrocyanide of potassium into the veins of horses,) the blood performs the circuit of the body in from 20 to 30 seconds. Several authorities are opposed to this statement. It is evident that the blood, as it issues from the heart, proceeds in smaller and larger circles; the smallest are those which it describes through the heart itself and the lungs, the larger are those through the extremities, and it must require different times to go over these different spaces, and besides this, its course is differently impeded in the capillary system of the different organs. Thus one portion of the blood may frequently pass through the heart and lungs, while another portion has only made one complete circuit, and traces of the injected ferrocyanide of potassium which permeates uniformly the whole mass of the blood, may therefore be found after a short time in parts of the system remote from the heart, which have not gone the perfect circuit through the heart, lungs, and all the organs. This appears to be very evident from the fact that some of those salts which are supposed to be rapidly eliminated by the kidneys, may be detected for a considerable period in the blood. Thus I observed,<sup>2</sup> that when iodide of potassium was taken at four o'clock in the afternoon, its presence was traceable in the urine till nine the next morning; and Hering<sup>3</sup> found ferrocyanide

<sup>1</sup> Treviranus *Zeitschrift für Physiologie*, 1832, p. 85.

<sup>2</sup> Simon, *Die Frauenmilch nach ihrem chemischen und physiologischen Verhalten*. Berlin, 1838, p. 75.

<sup>3</sup> *Op. cit.* p. 96.

anide of potassium in the urine of a horse two days after it had been injected. Hence the whole mass of the blood occupies a considerable time in passing through the renal arteries, or else the kidneys do not remove all the foreign constituents from the blood that passes through them.

Others have calculated the rapidity of the circulation by the quantity of blood projected by the heart at each systole. Reckoning this quantity at from 1 to 2 ounces, and the whole amount of blood in the human body at 30 pounds, it would take from 3 to 7 minutes (assuming the pulse to be 75 in the minute) for all this blood to pass through the heart. Since, however, the blood in the smaller circles passes more frequently through the heart in a given time than the blood in the larger circles, and since it is variously impeded and delayed in the different organs, we must not consider that the absolute mass of the blood of the whole body is represented by the identical 30 pounds which pass through the heart in from 3 to 7 minutes. The quantity of blood in an adult has likewise never been accurately determined. Hales places it at 25 pounds; the maximum is, however, calculated to amount to 30 pounds; and when we consider the extremely large quantity of blood that is retained in the capillary vessels, this estimate is probably too low.

That the rapidity with which the blood circulates varies inversely with the distance from the heart is an established fact. In the capillary system its progress is the most torpid. Omitting the consideration of the various mechanical impediments that meet the blood in the capillaries, it must be remembered that, if the blood is the real nutrient fluid of the body, there must be a necessary attraction between it and the organs it has to nourish. The blood in the capillary network permeates the tissues, or (to speak more correctly) the cells of the tissues attract from the blood their proper nutriment. It is clear that this must delay the course of the blood in the peripheral system, to what amount it is impossible to say, but in all probability the delay will vary directly with the intensity of the action between the blood and the tissues, and with the amount of the change of matter. The greatest delay will most probably occur in the kidneys and in the liver, since they afford the largest amount of secreted matters. Even if the amount of the secretions did not indicate a heightened cellular activity, it



would be sufficiently proved by the structure of the organs themselves, for they are permeated by such an extremely abundant and dense capillary network, and such very delicate venous twigs closely encircle their excretory ducts, that the tissue is brought in contact with the blood at every point and in every direction.

The chemical constitution of these organs is likewise so peculiar, that we might infer that the cells would exert a particular influence; for the muscular tissue, serous membrane, lung, &c. when triturated with water, yield little else than some of the constituents of the blood from the capillary vessels, while the liver and kidneys by trituration yield a pappy mass, which is for the most part soluble in water, contains much fat in a state of suspension, and leaves only a small amount of solid residue (18·9% in the liver, and, according to Berzelius, even less in the kidneys), consisting of shreds of vessels and membranes.

From the observations already made, we may infer that the blood undergoes a much more rapid metamorphosis in the kidneys and liver than in the tissues of the muscles, bones, &c. If it were possible to determine the time during which the same blood remains in these organs, then we might decide with some degree of certainty whether the blood which emerges from them differs in its composition from that which enters them. We have seen that there are reasons for assuming that the circulation is delayed in these organs. If we suppose, with Haller,<sup>1</sup> that the eleventh part of the whole blood passes through the kidneys, and that, consequently, at each systole of the heart four scruples are driven into them, then, assuming that the kidneys contain from four to six ounces of blood, and that the rapidity of the circulation in them is the same as in the aorta, the same blood will remain in these organs for about one third or one half of a minute. But taking into consideration the various facts that we have adverted to regarding the impeded circulation in these organs, we can scarcely doubt that the blood is detained in them for a very considerable period. According to a calculation made by Keil, and quoted by Hales in his 'Medical Statics,' the blood remains in the kidneys for several hours.

R. Wagner<sup>2</sup> measured the rapidity with which a blood-cor-

<sup>1</sup> Elem. Phys., vol. 2, p. 467.

<sup>2</sup> Lehrbuch der Physiologie, part 2, p. 193.



pulse moves in the capillary system, and found that it traversed a course of from 12 to 15 lines in the course of a minute. If the motion of the corpuscles and of the blood is supposed to be equal, and if the blood progresses in the large vascular trunks at the rate of eight inches in one second, and consequently 480 inches in one minute, then the rapidity of the blood in the larger trunks will be to the rapidity in the capillaries in the ratio of from 480—384 : 1 ; a calculation tending to show that the blood remains in the kidneys for a space of from one to two hours.

To this it may be objected that the phenomena of resorption are opposed to these results, and that if the renal veins convey away as much blood as is conducted to the kidneys by the renal arteries, this protracted delay would be impossible. We cannot, however, determine with certainty the amount of blood that enters the kidneys, for there is no necessity that the whole mass of the blood should flow through them as through the lungs ; moreover, only one branch of the aorta enters this viscus, and while the tendency of the blood is to flow in the direction in which it meets with the least opposition, there is, perhaps, no organ in the whole body that offers a greater resistance than the kidney. The chemical change that the blood undergoes in the kidneys must likewise be much more rapid than in the capillary vessels of many other tissues, since, in addition to the large amount of secretion that they yield, a portion of the consumed blood is carried away by the lymphatic vessels.

Let us now endeavour to ascertain how long it would be necessary for the blood to remain in the kidney, in order that the contents of the renal veins should exhibit chemical peculiarities dependent on the action of the gland. Assuming that a healthy man secretes about 40 ounces of urine in 24 hours, and that the change dependent on the secretion of 10 ounces of urine from 1000 ounces of blood may be detected by the changed proportion of the water, then, omitting all consideration of the lymphatic vessels, 4000 ounces of blood would pass through the kidney in 24 hours, in order to separate 40 ounces of urine. According to this calculation, 250 pounds of blood would pass through the kidneys in 24 hours, about 10 pounds in one hour, and 1 pound in six minutes ; and assuming that both kidneys

contain six ounces of blood, this blood must be retained in them for at least two minutes. This period is much shorter than those deduced by Keil and Wagner, in which it amounts to hours.

I think we may fairly conclude, from the preceding observations, that the changes which the blood undergoes in its composition while passing through the kidneys and liver, are appreciable; for if we have shown the probability of the correctness of the statement in the case of the kidneys, there can be no question that it is true in the case of the liver, which is everywhere permeated by the torpidly circulating blood of the vena portæ.

*On the absolute composition of healthy venous blood.*

It cannot be doubted but that the blood of different individuals in a state of perfect health will exhibit differences of composition, and that it would be the merest chance if the composition of the blood of two persons were found to be precisely the same. The circumstances capable of inducing a change in the composition of the blood are very numerous. Different methods of life, and various modes of nourishment, might cause such changes; but, independently of these external influences, there are others connected with the individual which must modify, to a greater or lesser degree, the composition of the blood, as, for instance, the influences of sex, age, and temperament.

It is extremely difficult to determine a formula for the composition of normal blood that would serve as a standard, by comparison with which we might detect absolute deviations in other forms and specimens of blood, on account of the variable nature of the fluid, changing even in the same individual at different periods of the day, and in accordance with the food that has been taken.

In a medical point of view, the composition of venous blood is the most interesting, because it is from the veins that blood is almost always taken in disease, and because venous blood can naturally only be compared with venous blood for the purpose of ascertaining any deviations that may occur.

Before attempting to give a decided opinion on the normal composition of venous blood, it would be requisite that numerous accurate analyses of the blood of healthy males and females

of different ages should be instituted. Possibly we should also regard the influence of their various modes of life, and (if we ascribe any influence to the circumstance) of their temperaments.

Experiments of this nature are still wanted, and the contributions hitherto made with that object by no means meet the exigencies of the case. Many difficulties present themselves in such an investigation.

It is not an easy matter to select individuals from whose state of health we can infer that the composition of the blood closely approximates to the normal standard, and after the selection is made it is still harder to convince them of the advantage or necessity of venesection in their own cases.

I was obliged to content myself with two such analyses, one of the blood of a young man, the other of an unmarried female.

Analysis 13. N—, aged 17 years, a servant, of sanguineous temperament, nearly full grown and properly developed, chest well arched, respiratory and digestive organs healthy, countenance florid and blooming, was bled from the arm. The blood was apparently rather brighter than usual, and when allowed to stand, separated into a bright red, uniformly coloured, copious, and properly consistent clot, and a clear bright yellow serum.

A portion of the blood was whipped as soon as it was drawn, and the analysis was conducted in accordance with my ordinary plan.

1000 parts contained :

Water . . . . .	791·900
Solid residue . . . . .	208·100
Fibrin . . . . .	2·011
Fat . . . . .	1·978
Albumen . . . . .	75·590
Globulin . . . . .	105·165
Hæmatin . . . . .	7·181
Extractive matter and salts . . . . .	14·174

100 parts of blood-corpuscles contained 6·3 of hæmatin and hæmaphæin.

Analysis 14. S—, a servant girl, aged 28 years ; temperament rather phlegmatic than sanguineous ; tall, strong, and vigorous ; countenance healthy ; digestion good ; had menstruated a fortnight before. The blood from the arm appeared rather dark, and on being left to itself separated into a considerable clot, and bright, clear yellow serum.

1000 parts of this blood contained:

Water	.	.	.	.	.	798·656
Solid residue	.	.	.	.	.	201·344
Fibrin	.	.	.	.	.	2·208
Fat	.	.	.	.	.	2·713
Albumen	.	.	.	.	.	77·610
Globulin	.	.	.	.	.	100·890
Hæmatin	.	.	.	.	.	5·237
Extractive matter and salts	.	.	.	.	.	9·950

100 parts of blood-corpuscles contained 5·2 of hæmatin and hæmaphæcin.

These two analyses indicate a great similarity between the blood in both sexes in a state of health; and if, in the absence of other and better experiments, we venture to take these as descriptive of the composition of normal blood, we may give its leading features in the following terms. *It contains about 20% of solid constituents; not much more than 0·2% of fibrin, and about an equal quantity of fat; the blood-corpuscles considerably exceed the albumen in quantity, and contain about 5% or 6% of colouring matter.*

Lecanu, although his method of analysing the blood is different, obtains similar results. He has given in his Thesis,<sup>1</sup> ten analyses of healthy venous blood, which I shall here communicate.

Age.	Water.	Solid residue.	Albumen.	Blood-corpuscles.	Extractive matter, salts, and colouring matter.
45	780·210	219·790	72·970	132·820	14·000
26	790·900	209·100	71·560	128·670	8·870
36	782·271	217·729	66·090	141·290	10·349
38	783·890	216·109	67·890	148·450	9·770
48	805·263	194·757	65·123	117·484	12·120
62	801·871	198·129	65·389	121·640	11·100
32	785·881	214·119	64·790	139·129	10·200
26	778·625	221·375	62·949	146·885	11·541
30	788·323	211·677	71·061	131·688	8·928
34	795·870	204·130	78·120	115·850	10·010

The mean of these analyses would give—

37	789·320	210·680	68·059	132·490	10·688
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From these analyses we therefore obtain about 21% of solid residue, and a larger proportion of blood-corpuscles than albumen. Lecanu assigns to the fibrin rather a larger proportion than I do, viz. 29%.

<sup>1</sup> Etudes chimiques sur le Sang humain, etc., p. 62.



The analyses of Denis, (although from the very different manner in which they were conducted, their results cannot very well be compared with mine,) upon the whole, support my statements with regard to the proportions in which the most important constituents occur.

I shall give some of his analyses in a condensed form, reducing them to the relative proportions of water, solid residue, fibrin, blood-corpuscles, and albumen.

The venous blood of healthy men contained in 1000 parts :

No. in Denis's work.	Age.	Water.	Solid residue.	Fibrin.	Albumen.	Blood-corpuscles.
46	21	733·0	267·0	2·3	55·0	182·9
56	25	732·0	268·0	2·5	60·0	181·4
13	31	766·0	234·0	2·1	62·2	149·2
42	36	758·0	242·0	2·0	62·0	155·0
9	40	733·0	267·0	2·7	52·3	186·0
38	50	748·0	252·0	2·5	55·0	170·6
57	54	770·0	230·0	2·3	57·0	145·3
14	65	800·0	200·0	3·1	60·0	114·8
15	70	790·0	210·0	2·7	56·0	131·6
41	78	781·0	219·0	2·5	61·0	130·4

The venous blood of women gave, in 1000 parts :

2	22	780·0	220·0	2·5	60·0	133·4
47	33	773·0	227·0	2·9	59·0	140·0
48	48	786·0	214·0	3·1	60·0	126·0
35	50	795·0	205·0	2·1	58·4	110·3

The venous blood of virgins gave, in 1000 parts :

39	22	814·0	186·0	2·7	60·0	100·0
33	38	774·0	226·0	2·7	68·4	131·5
29	48	760·0	240·0	2·7	50·0	162·4

In my observations on Denis's method of analysing blood I pointed out the reasons why some of the constituents would not be correctly determined. It is obvious that, in these analyses, two of my characteristics of healthy venous blood, namely, the proportions both of the solid constituents and of the blood-corpuscles are given in excess. I fix the proportion of the solid residue by an exact determination of the water, at about 20%, whereas these analyses would bring it up to 26·8%. Still greater discrepancies occur in the relative proportion of the albumen to the blood-corpuscles. In my analyses the proportion of the albumen to the hæmatoglobulin (the principal

constituent of the blood-corpuscles) is as 75:100 or 1:1.5. The proportion assigned by Lecanu is much the same, but approximates to the ratio 1:2; whereas Denis's proportion is usually 1:3 and often higher. Denis's amount of fibrin is larger than mine, but less than Lecanu's, for if the mean of the first 10 of his analyses be taken, the result is .24%.

In the estimation of the colouring matter there are, as might have been anticipated, considerable differences. The mean of my two analyses gives it as 6.2 in 1000 parts of blood; and in 100 parts of hæmatoglobulin the average is 5.7.

This quantity of colouring matter, when estimated, according to my method, from an analysis of 8—12 grains of dried blood, contains, moreover, hæmaphæin and some fat; in consequence of the very small proportion in which the two latter occur, (the former being frequently not more than from .14 to .3, and the latter about .3 of a grain,) I seldom attempted their separation unless I had reason to believe that a considerable quantity of hæmaphæin was present. The quantity of hæmatin, in my two analyses, is therefore placed rather too high. Lecanu estimates the hæmatin in 1000 parts of blood at 2.27, which is considerably less than half my average. This difference is owing partly to the circumstance of Lecanu's analyses being made with blood-corpuscles not thoroughly deprived of their fibrin, and which possibly retained a portion of moisture, and partly to the fact that Lecanu, by working on larger quantities, was enabled to remove all the hæmaphæin and fat. The average quantity of peroxide of iron in Denis's experiments amounted to .09%, which would correspond (according to my own and Lecanu's analyses,) with about 0.9 of hæmatin.

From the 10 analyses of man's blood, the mean quantity of blood-corpuscles is 15.8%. Hence Denis perfectly agrees with me in the consideration that the blood-corpuscles contain 5.7% of hæmatin.

I have not attempted any separation of the salts: Denis has, however, in all his analyses, determined the carbonates, phosphates, and chlorides.

It results from his important and elaborate observations, that although the relative proportions of the salts vary considerably, the limits to which they are restricted are not very

extended. I shall now give the quantity of the salts in the 10 analyses of man's blood, preserving the same order of succession as before.

1000 parts of healthy venous blood in a man contained:

No. in Denis's work.	Age.	Carbonate of soda.	Chloride of sodium.	Chloride of potassium.	Carbonate of lime.	Phosphate of lime, with traces of phosphate of magnesia.
46	23	2.0	4.9	3.9	2.8	0.6
56	25	2.0	4.2	3.6	2.6	0.8
13	31	1.2	4.0	2.1	1.2	0.7
42	36	1.0	4.0	3.1	2.0	0.3
9	40	2.1	5.2	2.3	1.8	0.4
38	50	1.3	4.9	2.5	1.3	0.5
57	54	2.0	4.2	3.5	2.7	0.5
14	65	2.1	5.0	1.0	1.3	0.2
15	70	1.0	4.0	2.1	1.3	0.5
41	78	1.5	4.2	3.2	1.7	0.5

The mean deduced from these 10 analyses is—

47	1.6	4.4	2.7	1.8	0.5
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And the average proportion of the salts, collectively, would be 11.1 in 1000 parts of blood.

[Nasse has analysed human blood, and found in 100 parts:

Water	. . . . .	798.402
Solid constituents	. . . . .	201.598
Fibrin	. . . . .	2.233
Fat	. . . . .	1.970
Albumen	. . . . .	74.194
Blood-corpuscles	. . . . .	116.529
Soluble salts	. . . . .	6.672

The soluble salts consisted of—

Alkaline phosphates	. . . . .	0.823
Alkaline sulphates	. . . . .	0.202
Alkaline carbonates	. . . . .	0.957
Chloride of sodium	. . . . .	4.690
		<hr/> 6.672

The insoluble salts were also estimated as follows:

Peroxide of iron	. . . . .	0.834
Lime	. . . . .	0.183
Phosphoric acid	. . . . .	0.201
Sulphuric acid	. . . . .	0.052
		<hr/> 1.270

The insoluble salts and extractive matters are probably included, in Nasse's analysis, in the albumen.

Becquerel and Rodier have recently published an elaborate memoir on the composition of the blood in health and disease. Their method of analysis is founded on nearly the same principles as that of Andral and Gavarret, which will be found at the commencement of our section on Diseased Blood.

The following table is drawn up from the analyses of the blood of 11 men, varying in age from 21 to 56 years, all of whom were considered by the experimenters to be in perfect health.

	Mean.	Max.	Min.
Density of defibrinated blood . . . . .	1060.2	1062.0	1058.0
Density of serum . . . . .	1028.0	1030.0	1027.0
Water . . . . .	799.0	800.0	760.0
Solid constituents . . . . .	201.0	240.0	200.0
Fibrin . . . . .	2.2	3.5	1.5
Fat <sup>1</sup> . . . . .	3.2	6.6	2.0
Albumen . . . . .	69.4	73.0	62.0
Blood-globules . . . . .	141.1	152.0	131.0
Extractive matters and salts . . . . .	6.8	8.0	5.0

1000 parts of incinerated blood contained :

	Mean.	Max.	Min.
Chloride of sodium . . . . .	3.10	4.20	2.30
Other soluble salts . . . . .	2.50	3.20	2.00
Earthy phosphates . . . . .	0.33	0.70	0.22
Iron . . . . .	0.56	0.63	0.51

The composition of the blood in the healthy female, as deduced from eight analyses, is given in the following table :

	Mean.	Max.	Min.
Density of defibrinated blood . . . . .	1057.5	1060.0	1054.0
Density of serum . . . . .	1027.4	1030.0	1026.0
Water . . . . .	791.1	813.0	773.0
Solid constituents . . . . .	208.9	227.0	187.0
Fibrin . . . . .	2.2	2.5	1.8
Fat <sup>2</sup> . . . . .	2.2	5.7	2.0
Albumen . . . . .	70.5	75.5	65.0
Blood-globules . . . . .	127.2	137.5	113.0
Extractive matters and salts . . . . .	7.4	8.5	6.2

<sup>1</sup> This fat contained :

	Mean.	Max.	Min.
Serolin . . . . .	0.020	0.080	inappreciable.
Phosphorized fat . . . . .	0.488	1.000	0.270
Cholesterin . . . . .	0.088	0.175	0.030
Saponified fat . . . . .	1.004	2.000	0.700

<sup>2</sup> This fat contained :

	Mean.	Max.	Min.
Serolin . . . . .	0.020	0.060	inappreciable.
Phosphorized fat . . . . .	0.464	0.800	0.250
Cholesterin . . . . .	0.090	0.200	0.025
Saponified fat . . . . .	1.046	1.800	0.725



1000 parts of the incinerated blood contained :

	Mean.	Max.	Min.
Chloride of sodium . . .	3.90	4.00	3.50
Other soluble salts . . .	2.90	3.00	2.50
Earthy phosphates . . .	0.35	0.65	0.25
Iron . . . . .	0.54	0.57	0.48

The salts have been analysed by Marchand. They amount (he observes) to 6.28—6.82% of the dried residue. The four following analyses are given in his '*Lehrbuch der Physiologischen Chemie* :'

	1.	2.	3.	4.
Chloride of sodium . . .	3.91	3.42	3.81	3.82
Chloride of potassium . .	0.32	0.21	0.31	0.38
Carbonate of soda . . .	0.62	0.52	0.72	0.61
Sulphate of soda . . .	0.31	0.52	0.38	0.42
Phosphate of soda . . .	0.56	0.72	0.68	0.59
Phosphate of lime . . .	0.25	0.31	0.28	0.30
Phosphate of magnesia . .	0.21	0.20	0.25	0.28
Lactate of soda . . .	0.32	0.28	0.35	0.34
Lactate of ammonia . . .	0.12	0.10	0.00	0.08
	6.62	6.28	6.78	6.82

In 100 parts of the ash of human blood there are contained, according to Enderlin :

Tribasic phosphate of soda ( $3\text{Na}, \text{PO}_5$ ) .	22.100	} = 83.740 soluble salts.
Chloride of sodium . . . . .	54.769	
Chloride of potassium . . . . .	4.416	
Sulphate of soda . . . . .	2.461	
Phosphate of lime . . . . .	3.636	} = 15.175 insoluble salts.]
Phosphate of magnesia . . . . .	0.769	
Peroxide of iron and phosphate of iron .	10.770	

*On the differences of the blood, dependent on sex.*

Lecanu<sup>1</sup> concludes from his analyses that the venous blood of males is richer in solid constituents than that of females, but that the quantity of albumen in both is the same. The following are the maxima, minima, and mean results of his analyses :

	Water in venous blood of men.	Ditto in that of females.
Maximum . . . . .	805.263	853.135
Minimum . . . . .	778.625	790.394
Mean . . . . .	791.944	821.764
	Albumen in ditto.	Albumen in ditto.
Maximum . . . . .	78.270	74.740
Minimum . . . . .	57.890	59.159
Mean . . . . .	68.080	66.949

<sup>1</sup> Etudes chimiques, etc., p. 65 ; or Journal de Pharmacie, vol. 18, p. 551.

Having only made two analyses of the blood of healthy persons, I am not in a position to draw any inferences regarding differences in its composition, dependent upon sex. I have, however, deduced, from Denis's analyses, a table indicating the differences that exist between male and female blood, at the same age.

<i>Blood of Males :</i>	Water.	Blood-corpuscles.	Albumen.	Fibrin.
Maximum . .	790.0	187.1	63.0	2.9
Minimum . .	733.3	102.0	52.3	2.1
Mean . .	758.0	147.0	57.5	2.5
<i>Blood of Females :</i>				
Maximum . .	820.0	162.4	66.4	3.0
Minimum . .	750.0	88.1	50.0	0.25
Mean . .	773.0	138.0	61.2	0.27

Hence it appears that the analyses of Denis<sup>1</sup> bear out Lecanu's statement with regard to the smaller proportion of water in male than in female blood: the albumen, however, appears to be rather more abundant in female than in male blood. The proportion of blood-corpuscles is smaller, and of fibrin rather larger than in the blood of the male.

[From the analyses of Becquerel and Rodier, it appears that the influence of sex is so great, that, in order to arrive at any correct conclusions respecting the deviation of morbid blood from the healthy standard, diseased male and female blood must be always contrasted with the respective male and female blood in a state of health. The mean differences may be seen by a glance at the following table :

	Male.	Female.
Density of defibrinated blood . . . . .	1060.0	1057.5
Density of serum . . . . .	1028.0	1027.4
Water . . . . .	779.0	791.1
Fibrin . . . . .	2.2	2.2
Sum of fatty matters . . . . .	1.60	1.62
Serolin . . . . .	0.02	0.02
Phosphorized fat . . . . .	0.488	0.464
Cholesterin . . . . .	0.088	0.090
Saponified fat . . . . .	1.004	1.046
Albumen . . . . .	69.4	70.5
Blood-corpuscles . . . . .	141.1	127.2
Extractive matters and salts . . . . .	6.8	7.4
Chloride of sodium . . . . .	3.1	3.9
Other soluble salts . . . . .	2.5	2.9
Earthy phosphates . . . . .	0.334	0.354
Iron . . . . .	0.566	0.541

<sup>1</sup> Op. cit. p. 290.

Hence female blood differs materially from the blood of the male in the amount of water and of blood-corpuscles.]

*On the differences of the blood, dependent on constitution.*

Denis concludes from his analyses that, generally speaking, the stronger the constitution is, the greater will be the amount of solid constituents, and especially of blood-corpuscles. If age is also taken into consideration, my observations confirm those of Denis. At equal ages, the blood in weak constitutions is less abundant in solid constituents and hæmatoglobulin than in stronger constitutions.

*On the differences in the blood, dependent upon temperament.*

According to Lecanu,<sup>1</sup> temperament has an influence upon the composition of the blood. He infers from his analyses that the blood of lymphatic persons is poorer in solid constituents, and especially in blood-corpuscles, than that of persons of sanguineous temperament, while the quantity of albumen is much the same in both. The following table will illustrate these views.

1000 parts of blood contained on an average :

	Men of sanguineous temperament.	Men of lymphatic temperament.
Water . . . .	786.584	800.566
Albumen . . . .	65.850	71.781
Blood-corpuscles . .	136.497	116.667
	Women of sanguineous temperament.	Women of lymphatic temperament.
Water . . . .	793.007	803.710
Albumen . . . .	71.264	68.660
Blood-corpuscles . .	126.174	117.300

*On the differences in the blood, dependent on age.*

My own observations, which, however, chiefly refer to diseased blood, lead to the conclusion that the blood of young persons contains a larger proportion of solid constituents, and especially of blood-corpuscles, than that of older persons. Lecanu and Denis have, however, made this a point of especial inquiry, and have extended their analyses over a wide range of ages.

<sup>1</sup> Op. cit. p. 66.

I have drawn up the following table from the numerous analyses of Denis, the blood being considered healthy.

1000 parts of healthy blood of males contained :

Age.	Water.	Solid residue.	Fibrin.	Blood-corpuscles.	Albumen.
14 years.	750·4	249·6	4·0	162·2	58·0
23	733·0	267·0	2·3	182·9	55·0
25	732·0	268·0	2·5	181·4	60·0
31	766·0	234·0	2·1	150·1	62·2
33	783·0	217·0	2·9	129·3	60·0
40	750·0	250·0	2·5	167·8	55·1
46	769·0	231·0	2·5	156·9	48·5
50	748·0	252·0	2·5	170·9	55·0
53	790·0	210·0	2·6	100·0	63·0
54	798·0	202·0	3·0	111·0	63·0
65	800·0	200·0	3·1	114·8	60·0
70	790·0	210·0	2·7	132·3	56·0
80	781·0	219·0	2·5	130·4	61·0

1000 parts of healthy blood of females contained :

4	833·0	167·0	2·8	80·5	64·0
6	820·0	180·0	2·5	97·6	59·0
12	787·0	213·0	2·3	130·0	57·0
15	774·0	226·0	2·5	135·7	65·0
20	772·0	228·0	2·5	144·2	57·0
22	780·0	220·0	2·5	133·4	60·0
32	750·0	250·0	3·0	173·4	51·0
38	774·0	226·0	2·7	131·5	68·4
48	786·0	214·0	3·1	126·0	60·0
52	820·0	180·0	2·9	88·1	68·0
74	745·0	255·0	2·5	171·1	55·0

It appears from these tables, especially from the second, that the blood is less abundant in solid constituents, and particularly in blood-corpuscles in early life, than at the period of maturity. From the latter period (or rather sooner) to middle life the proportions of the corpuscles and of the solid constituents continues large ; from that time to an advanced age they are subject to a decrease. [Becquerel and Rodier observe that, after the age of 40 or 50, there is a decided and progressive increase of cholesterin in the blood.]

Denis has made a comparative analysis of the blood of the mother and of the foetus ; he found that the latter was richer in solid constituents and in blood-corpuscles than the former.



The two following analyses, one of the venous blood of the mother, the other of the placental blood as it issued from the artery of the cord, may serve as an additional illustration of the point.

The blood of the umbilical artery was of a brown-red colour, smelled of the liquor amnii, and became of a brighter colour on being exposed to the air.

	Venous blood of mother.	Blood of umbilical artery.
Water . . . . .	781.0	701.5
Solid residue . . . . .	219.0	298.5
Fibrin . . . . .	2.4	2.2
Albumen . . . . .	50.0	50.0
Blood-corpuscles . . . . .	139.9	222.0
Peroxide of iron . . . . .	0.8	2.0
Phosphorized fat . . . . .	9.2	7.5
Osmazome and cruorin . . . . .	4.2	2.7
Salts . . . . .	12.5	12.1

The difference in the solid constituents and in the blood-corpuscles is obviously very considerable; the same is the case with the iron, the ratio being 1 to 2.5.

The mass of the blood in the fœtus increases in a very rapid ratio with the development. The proportion of corpuscles is more augmented, and the quantity of water is less than occurs at any subsequent period of life. Even for some time after birth the mass of the blood is relatively large, and the proportion of blood-corpuscles and of iron contained in them is considerably above the ordinary standard.

Denis has made some experiments on the difference between the blood of very young animals and those of mature age, which confirm the observations already made. His experiments were instituted on dogs.

	Blood of a dog, 3 months old.	Blood of a puppy, 1 day old.
Water . . . . .	830.0	780.0
Solid residue . . . . .	170.0	220.0
Fibrin . . . . .	2.4	2.0
Albumen . . . . .	58.6	46.0
Blood-corpuscles . . . . .	97.0	165.0
Extractive matter and salts . . . . .	12.0	7.0

When the skin of the new-born animal loses its red tint, the blood becomes more watery, the blood-corpuscles and the quantity of iron are diminished, and it becomes relatively, but

not absolutely, poorer, for its quantity at the same time increases. Subsequently, however, when the generative powers begin to be developed, the corpuscles and the iron increase, and the relative proportion of water diminishes. At the period of full development the excess of corpuscles and iron serve in maintaining the necessary energy of that part of the system, and till the generative powers begin to flag the blood remains abundant in solid constituents, and more especially in corpuscles.

These observations are suggested by the results obtained by Denis,<sup>1</sup> as will be clearly seen by the following table, which was drawn up by that chemist himself.

The mean amount of solid constituents and of blood-corpuscles at different ages are given in the following proportions.

				Solid constituents.	Blood-corpuscles.
In 5 individuals between 5 months and 10 yrs.				170	11
13	"	10 years and 20 yrs.		200	14
11	"	20		30	240
12	"	30	40	240	17
6	"	40	50	240	17
8	"	50	60	220	15
2	"	60	70	210	14

The following table shows that Lecanu's analyses confirm those of Denis and myself.

Age.	Water.	Solid residue.	Blood-corpuscles.	Albumen.
26	778·625	221·375	146·885	62·949
30	788·323	211·677	131·688	71·061
34	795·870	204·130	115·850	78·120
38	783·890	216·110	148·450	67·890
45	780·210	219·790	132·820	72·970
48	805·263	194·737	117·484	65·123
62	801·871	198·129	121·640	65·389

#### ON DISEASED BLOOD.

##### *The pathological chemistry of the blood.*

The question whether there exists such a thing as *diseased blood* is easily answered. The material deviations from its normal condition exhibited by the blood in its physico-chemical relations, in certain morbid conditions of the system, have long been recognized by pathologists.

<sup>1</sup> Recherches, pp. 289, 290.

The quantity of the fibrin is sometimes found to be very much increased, while in other cases it is present only in such very small proportions that no clot is formed. The blood will sometimes be found to be very rich in solid constituents, and especially in blood-corpuscles; while at other times it will be so poor as to resemble coloured water. In some instances the corpuscles will sink rapidly in whipped blood; while in others they will only deposit themselves slowly and imperfectly, so that merely a thin layer of serum remains above them. It will also sometimes contain substances which are not found in it in a normal state, as colouring matter of the bile, sugar, or urea. All these are deviations from the normal state of the blood; and if we term that blood healthy, which is constituted in the ordinary manner, and properly discharges its various functions, we are perfectly justified in considering blood as diseased which does not fulfil these conditions.

The analyses published by Andral and Gavarret,<sup>1</sup> in their elaborate essay upon this subject, correspond in their results, generally speaking, with those instituted by myself. They, however, usually assign a higher proportion to the corpuscles (especially in the blood during inflammatory diseases) than I have found to occur. It is hardly probable that such differences should arise from the geographical positions of the observers, although, generally speaking, the blood may be richer in solid constituents and in corpuscles, in southern than in northern regions: it is more likely that they are caused by the different methods of analyses pursued by the French observers and myself. I have tried both methods, and consider it useful, if not necessary, to state the results of my trial.

In the analyses of Andral and Gavarret, the blood is received into two six-ounce vessels. The first and fourth quarters are received in one vessel, the second and third in the other. In one, the blood is allowed to coagulate spontaneously; in the other, it is whipped, in order to obtain the fibrin, which must be carefully washed. When the coagulation is effected, the clot must be carefully removed from the serum, and we must dry (*a*) the fibrin which has been obtained by whipping one portion of the blood; (*b*) the serum; and (*c*) the clot. By weighing

<sup>1</sup> *Annal. de Chimie et de Phys.* vol. 75, p. 225.

the dried fibrin we know the quantity of that constituent contained in the clot. By weighing the dried serum we know the proportions of water and of solid constituents contained in it. Lastly, we weigh the dried clot: the quantity of water which it gives off is estimated as serum, and the solid residue due to it is readily calculated. By deducting from the weight of the dried clot the weights of the fibrin and of the solid residue of the serum contained in the clot, we obtain the amount of the globules. Hence we have (1) the weight of the fibrin; (2) the weight of the globules; (3) the weight of the solid residue of the serum; and (4) the weight of the water.

This method is simple, and easy of application, in cases in which it is unnecessary to ascertain the proportions of hæmatin, globulin, fat, hæmaphæin, extractive matters, and salts, separately. I shall, however, show that an error may easily arise in the determination of the blood-corpuscles, if the drying has not been perfectly effected.

In order to ascertain what would be the amount of differences, I analysed the same blood by their method, and by my own. About eight ounces of blood were received in a glass, from the arm of a woman, aged 35 years. It was rapidly stirred; about a fourth part of it was poured into a small glass, and the fibrin removed in the ordinary manner, by whipping. The larger portion was left to coagulate.

#### 1. *Analysis of the defibrinated blood.*

The blood, including the fibrin, weighed 950 grains, of which the fibrin, when washed and thoroughly dried, weighed 1·9 gr. Hence 1000 parts of blood contain 2·0 of fibrin.

112·42 grains of defibrinated blood left, after the thorough removal of the water, a solid residue, amounting to 20·33 grs.

Hence 1000 parts of blood contained 180 of solid constituents; 7·7 grains of the dried residue were boiled in spirit of ·925, to which three drops of dilute sulphuric acid were subsequently added, as long as the spirit continued to take up anything more, and until a bright gray-green residue was left. This residue, which is composed of the albumen of the blood, when dried, weighed 3·31 grains.

The red alcoholic solution was saturated with ammonia, and evaporated to a small residue. The hæmatoglobulin, which se-



parated perfectly in this way, was then washed several times with water, dried, and weighed. Its weight amounted to 4 grains. The extractive matters and salts (including loss) may therefore be estimated at  $\cdot 39$  of a grain.

Now since 1000 parts of the defibrinated blood contain 180 of solid residue, the blood must contain :

Water . . . . .	818·00
Solid residue . . . . .	182·00
<hr/>	
Fibrin . . . . .	2·00
Albumen . . . . .	77·40
Hæmatoglobulin . . . . .	93·60
Extractive matters, salts, and loss . . . . .	9·00
<hr/>	
	1000·00

11. *Analysis of coagulated blood, according to the method of Andral and Gavarret.*

*a.* The serum weighed 1406 grains.

*b.* The clot weighed 1228 grains.

In order to ensure a greater degree of accuracy in my results, I evaporated only a portion of this quantity.

375·14 grains of the clot when dried, cautiously pulverised, and again heated, left 112·54 grains. Hence 100 parts of the clot contained 30·0 of solid constituents. 449·98 grains of serum left 42·66 of solid residue, which corresponds therefore with 9·5%.

1000 parts of blood consist of 533·8 of serum and 466·2 of clot, of which the serum gives a residue of 50·7, and the clot of 139·86 parts. The solid residue of 1000 parts amounts therefore to 190·56.

From the residue of the clot we deduct 2·0 for fibrin, and 31·0 for the solid residue of the serum contained in it, which must be added to the 50·7. Consequently 1000 parts of blood contain :

Water . . . . .	809·44
Solid residue . . . . .	190·56
<hr/>	
Fibrin . . . . .	2·00
Solid residue of serum . . . . .	79·70
Blood-corpuscles . . . . .	108·86
<hr/>	
	1000·00

The differences between these analyses are obvious. The solid constituents obtained by Andral and Gavarret's method are 8·5 higher, in 1000 parts of blood, than by mine; moreover, the quantity of corpuscles obtained by them considerably exceeds the hæmatoglobulin separated by my method. If we assume that the 8·5 parts of water which Andral and Gavarret's method did not succeed in removing, were retained in the clot, the corpuscles would be reduced from 108·86 to 98·3; in which case the discrepancy between the two analyses would be much less striking.

1000 parts of blood would then contain :

<i>According to Simon.</i>		<i>According to Andral and Gavarret.</i>	
Fibrin	2·00	Fibrin	2·00
Albumen, with extractive matters, and salts	86·40	Solid residue of serum	80·50
Hæmatoglobulin	93·60	Blood-corpuscles	99·50

It must, however, be remarked, that the sum of the hæmatin and globulin, in my analyses, can never represent the absolute quantity of blood-corpuscles. As has been previously remarked, the nuclei and capsules of the blood-corpuscles have been estimated as albumen by my method, as fibrin by Berzelius, and as appertaining to the corpuscles by Andral and Gavarret.

Their absolute weight has never been accurately ascertained,<sup>1</sup> but it cannot be larger, since the quantities of fibrin obtained by washing the clot, and by whipping fresh blood differ very little. Further, a portion of fat separated by my method, belongs to the blood-corpuscles, and we cannot deny the possibility of the corpuscles containing albumen.

My analyses, moreover, aim not merely at the determination of the proportion of the fibrin, of the corpuscles, and of the solid residue of the serum, but they are intended to embrace the determination of the most important proximate constituents of the blood; and if the hæmatoglobulin, or possibly the globulin be regarded as constituting the principal mass of the corpuscles, I can succeed in tracing their increase or decrease by means of the proportion of the hæmatoglobulin or globulin.

The following objections may likewise be brought against Andral and Gavarret's method.

<sup>1</sup> Nasse (*Das Blut in mehrfacher Beziehung*, &c., Bonn, 1836, p. 109) has attempted to form a quantitative analysis of the nuclei.

In cases where no consistent clot is formed, but where there is merely a slight gelatinous coagulation, as frequently occurs in blood deficient in fibrin, the serum and the clot cannot be separated with any degree of exactness. If the clot be allowed to stand for some hours in order to induce a more perfect separation of the serum, the water partially evaporates, and the ratio of the solid constituents of the clot to the water becomes changed, and consequently too high a number is assigned to the corpuscles. The difficulty of thoroughly removing the water varies in a direct proportion with the quantity of the blood submitted to evaporation. Serum, comparatively poor in solid constituents, gives only a slight residue, from which the water can be more readily expelled, than from the more abundant residue left by the clot: in proportion to the water remaining in the clot, the quantity of corpuscles found by this method will be increased, as will be clearly seen by the following illustration.

1000 parts of blood are composed of 500 parts of serum and 500 of clot.

The serum leaves a solid residue of 50, or 10%; the clot of 150, or 30%.

The 350 parts of water in the clot are to be estimated as serum, and thus give a residue of 35 parts; so that 1000 parts of blood, (the fibrin not being taken into consideration) consist of:

Water . . . . .	800
Solid residue . . . .	200
Blood-corpuscles . . .	115
Residue of serum . . .	85

If, however, the clot had not been perfectly dried, and if only 1 per cent. of water in relation to the weight of the whole blood had been retained, we should have obtained the following result :

500 parts of clot would then give 160 of solid residue, and there would therefore be 340 of water, which, estimated as serum, would yield 34 of residue; consequently the corpuscles would be estimated at 126, and 1000 parts of blood would consist of :

Water . . . . .	790
Solid residue . . . .	210
Blood-corpuscles . . .	126
Residue of serum . . .	84

In all other methods of analysing the blood in which the water is determined by a separate process, and the dried residue is used for further investigation, an error in its estimation will simply increase the absolute quantity of the solid constituents, without disturbing their relative proportions. But in the application of their method it is easy to see that each per-centage of retained water not only increases the absolute quantity of the solid constituents to the amount of 1%, but also the weight of the corpuscles, not only by the addition of the retained water, but also by the weight of the residue of the serum, due to an equal quantity of water, and which amounts to 1.1%.

Moreover, the supposition of Andral and Gavarret, that the humidity of the clot should be considered as serum is totally devoid of foundation. The corpuscles cannot be supposed to swim in the plasma as dry molecules, and it has not been proved that the fluid, with which they are filled, is the fluid of the serum.

These observations are sufficient to show that Andral and Gavarret's method, and my own, give somewhat different results: the differences, however, are not very material, and are easily explicable on the grounds already stated.

The changes which the composition of the blood may experience in its various pathological conditions, are either dependent upon the quantity of solid residue generally, or upon the changed relative proportions that the various proximate constituents bear to each other.

If we assume the composition of healthy blood, (as deduced from the mean of my analyses) to be represented by

Water	.	.	.	.	795.278
Solid residue	.	.	.	.	204.022
Fibrin	.	.	.	.	2.104
Fat	.	.	.	.	2.346
Albumen	.	.	.	.	76.600
Globulin	.	.	.	.	103.022
Hæmatin	.	.	.	.	6.209
Extractive matters and salts					12.012,

the following differences will be found to occur among the specimens of diseased blood which I have analysed. The quantity of—



Water . . .	may vary from 888.0	to 750.0
Solid residue . . .	250.0	112.0
Fibrin . . .	9.1	a trace
Fat . . .	4.3	0.7
Albumen . . .	131.0	55.1
Globulin . . .	106.6	30.8
Hæmatin . . .	8.7	1.4
Hæmatoglobulin . . .	115.4	31.2
Extractive matters and salts . . .	16.5	7.6

The analyses of the French chemists gave the following results, with regard to this subject.

Taking the mean of Lecanu's analyses of healthy blood as a standard, and contrasting with it the extreme results which were found by Andral and Gavarret in diseased blood, we have the following results:

*Lecanu's Analysis.*

Water . . . . .	790
Solid residue . . . . .	210
Fibrin . . . . .	3
Organic residue of serum . . . . .	72
Inorganic ditto . . . . .	8
Blood-corpuscles . . . . .	127

*Andral and Gavarret's Deviations.*

Water . . . . .	from 915.0	to 725.0
Solid residue . . . . .	275.0	85.0
Fibrin . . . . .	10.5	0.9
Solid residue of serum . . . . .	114.0	57.0
Blood-corpuscles . . . . .	185.0	21.0

From these data, it appears, that although the proportions of all the constituents are subject in disease to a certain amount of change, the variation is the most striking with regard to the fibrin and globulin.

The former is found in my analyses occasionally to exceed four times the average quantity, and in Andral and Gavarret's, three and a half times; while the latter may diminish, according to my analyses, to a mere trace; and according to Andral and Gavarret's, to one sixth of the normal quantity.

These determinations must not, however, be regarded as absolute: they are dependent on various causes, and can be explained in more ways than one.

For instance, the 21 parts of blood-corpuscles were observed by Andral and Gavarret in blood which left a residue of only 85, while the 185 of corpuscles occurred in blood which gave a residue of 275. Hence the per-centages of the corpuscles in these two cases, in regard to the solid residue, are 25% and 67% respectively.

The deviations in the proportions of the various constituents do not occur singly, for instance, we do not find the other constituents in normal proportions, and the blood-corpuscles alone very low; neither are they all found simultaneously deficient or in excess: but there exists, as we shall soon see, a certain antagonism between the proportions of the individual constituents. Thus we find that when the fibrin is much increased, the corpuscles are diminished in quantity, and *vice versa*.

In every 100 parts of the residue of healthy blood, we have 1 of fibrin and 53 of hæmatoglobulin. In diseased blood I have observed the following proportions:

Fibrin.	Hæmatoglobulin.
1·4	43
1·6	40
1·7	40
2·0	42
2·0	39
2·1	36
3·0	28
6·0	22

A similar relationship is exhibited in the analyses of Andral and Gavarret; the range of the corpuscles is, however, not so extensive.

	Fibrin.	Blood-corpuscles.
Healthy blood . .	1·5	61
Diseased blood . .	2·5	60
„ . .	3·2	57
„ . .	4·1	57
„ . .	4·2	54
„ . .	4·8	52
„ . .	5·0	50

The connexion between the fibrin and blood-corpuscles is still more strikingly exhibited in some of the analyses of Andral and Gavarret, in which blood was taken several successive times

from the same patient. We select four cases by way of illustration :

<i>Venesection.</i>	Fibrin.	Blood- corpuscles.	Fibrin.	Blood- corpuscles.	Fibrin.	Blood- corpuscles.	Fibrin.	Blood- corpuscles.
1st	6·3	130	6·1	123	4·0	111	5·6	133
2d	7·7	106	7·2	120	5·5	107	5·5	131
3d	8·2	112	7·8	112	6·5	101	9·1	128
4th	9·3	103	10·2	101	9·0	83	9·4	102

In the following table drawn up from Andral and Gavarret's analyses, the first column gives the proportions of fibrin and of corpuscles in 100 parts of solid residue. The second column does the same, only that in this case the quantity of fibrin is considered constant, and is represented by 1·5, and the proportion of corpuscles is estimated accordingly : an arrangement which makes their increase more obvious.

	Fibrin.	Corpuscles.	Fibrin.	Corpuscles.
Healthy blood	1·5	61	1·5	61
Diseased blood	1·5	64	1·5	64
"	1·5	65	1·5	65
"	1·3	60	1·5	69
"	1·1	53	1·5	72
"	1·2	59	1·5	74
"	1·1	60	1·5	81
"	1·0	60	1·5	90
"	0·9	60	1·5	90
"	1·0	61	1·5	91
"	1·0	64	1·5	96
"	0·9	63	1·5	105
"	0·5	60	1·5	180

[Becquerel and Rodier have laid it down as a general law that "bleeding exerts a remarkable influence on the composition of the blood, the greater the oftener the bleeding is repeated." The three following tables show the mean results of the first, second, and third venesections, performed on a certain number of Cruveilhier's patients. Ten patients were bled twice, and ten thrice, so that we have 20 first, 20 second, and 10 third bleedings.

*Mean composition of the blood of twenty persons bled twice.*

	1st Venesection.	2d Venesection.
Density of defibrinated blood . . . . .	1055·0	1051·2
Density of serum . . . . .	1026·1	1025·3
Water . . . . .	796·2	812·0
Solid residue . . . . .	203·8	188·0
Fibrin . . . . .	3·7	3·8
Albumen . . . . .	66·2	62·5
Blood-corpuscles . . . . .	125·4	112·0
Extractive matters and salts . . . . .	6·8	7·6
Fat . . . . .	1·657	1·560
Consisting of—Serolin . . . . .	0·027	0·047
Phosphorized fat . . . . .	0·490	0·465
Cholesterin . . . . .	0·178	0·150
Saponified fat . . . . .	0·962	0·900

The salts in 1000 parts of blood were :

Chloride of sodium . . . . .	2·8	3·4
Other soluble salts . . . . .	2·7	2·5
Phosphates . . . . .	0·435	0·417
Iron . . . . .	0·527	0·488

*Mean composition of the blood of ten persons bled three times.*

	1st Venesection.	2d Venesection.	3d Venesection.
Density of defibrinated blood . . . . .	1056·0	1053·0	1049·6
Density of serum . . . . .	1028·8	1026·3	1025·6
Water . . . . .	793·0	807·7	833·1
Solid residue . . . . .	207·0	192·3	176·9
Fibrin . . . . .	3·5	3·8	3·4
Albumen . . . . .	65·0	63·7	64·6
Blood-corpuscles . . . . .	129·2	116·3	99·2
Extractive matters and salts . . . . .	7·7	6·9	8·0
Fat . . . . .	1·662	1·584	1·530
Consisting of—Serolin . . . . .	0·026	0·088	0·012
Phosphorized fat . . . . .	0·637	0·489	0·450
Cholesterin . . . . .	0·106	0·156	0·149
Saponified fat . . . . .	0·893	0·851	0·919

The salts contained in 1000 parts of blood were:

Chloride of sodium . . . . .	2·8	3·5	3·0
Other soluble salts . . . . .	2·6	2·5	2·7
Phosphates . . . . .	0·404	0·493	0·348
Iron . . . . .	0·513	0·471	0·468

From these tables they draw the following conclusions. "In proportion to the number of venesections the blood becomes impoverished and more watery; hence the fall in the density of the defibrinated blood. The albumen diminishes, but only slightly;



hence the density of the serum is not much affected. The fibrin is quite uninfluenced by venesection, and its amount is determined by the nature and intensity of the disease. The extractive matters and salts are unaltered. There is a slight diminution in the amount of fat. The various salts are unaffected, and the iron, in consequence of its relationship to the corpuscles, is diminished. In short, the effect of venesection is to cause a great diminution of the corpuscles, while it only slightly lessens the amount of albumen.”]

#### THE FIRST FORM OF DISEASED BLOOD, HYPERINOSIS.<sup>1</sup>

##### *Chemical characters of the blood.*

The blood contains more fibrin than in the normal state, and the corpuscles decrease in proportion to the excess of fibrin; the fat is also increased. In proportion to the increase of the fibrin and fat, and the decrease of the corpuscles, the whole solid residue will be diminished.<sup>2</sup>

##### *Physical characters of the blood.*

The blood coagulates more slowly than in the normal state; the clot is usually not small, but very firm and consistent, and does not break up for a considerable time. It is almost invariably covered with a true buffy coat, (which is produced by the sinking of the corpuscles before the occurrence of coagulation, and by the subsequent coagulation of the fibrin in the layer of serum.)<sup>3</sup> This buffy coat is firm, tough, and intimately connected with the clot; its edge is often turned upwards, and its surface uneven.<sup>4</sup> If the clot is small, the buffy coat and

<sup>1</sup> Derived from *ὕπερ* and *ἵνως*, the fibre of flesh.

<sup>2</sup> Nasse (Das Blut in mehrfacher Beziehung, &c.) has arrived at similar conclusions; for he observes that the corpuscles and the fibrin are generally in an inverse ratio, and that blood exhibiting a decided genuine buffy coat is usually of low specific gravity, that is to say, the amount of water is increased.

<sup>3</sup> [The buffy coat does not consist of true fibrin, but of the binoxide and tritoxide of protein. (See page 10.)]

<sup>4</sup> The buffy coat is not exclusively connected with an inflammatory state of the blood; it occurs in other diseases, as, for instance, in chlorosis, but its properties are then very different. A very elaborate disquisition on the formation, and the proximate and remote causes of the buffy coat, occurs in Nasse's work, pp. 36-57, and 204-240.

the surface of the clot are more or less cupped; the serum is of a pure lemon colour, not tinged red. When subjected to whipping, the fibrin separates in thicker and more solid masses than in ordinary blood. After the removal of the fibrin the corpuscles quickly sink, and frequently occupy only one fourth of the whole fluid, while, in healthy blood, they sink very imperfectly or not at all. The blood has always an alkaline reaction, and is of a higher temperature than in the ordinary state.

Lauer<sup>1</sup> found the temperature of the blood in pneumonia as high as 100°, and in bronchitis it reached 101°·6. These temperatures are, however, not higher than are met with in healthy blood.

According to Becquerel the temperature may rise to 50°·4 in inflammatory diseases and fevers.

According to Cupil it amounts, in inflammatory disorders, to 106°—111°·7, and at the inflamed region to 112°·4.

The microscope has not yet succeeded in detecting any constant peculiarities.

The blood occurs in a state of hyperinosis in all inflammatory disorders (Phlogoses).

In proportion to the firmness of the clot, the concavity of its surface, (the cupping,) and the toughness, and thickness of the buffy coat, is the degree of inflammation; and conversely the thinner and more friable the clot is, the less intense is the disorder. We also find, accompanying these physical symptoms, an excess of fibrin, and a diminution of hæmatoglobulin, as well as of the solid constituents of the blood generally, and in proportion to the degree in which these phenomena are observed, we may infer a greater or lesser amount of inflammatory action.

[Before proceeding to the consideration of individual diseases, we may observe that Becquerel and Rodier have deduced the following law from their numerous analyses of morbid blood. "The development of an inflammatory disorder produces remarkable modifications in the composition of the blood, of which the most striking is the increase of fibrin."<sup>2</sup>

<sup>1</sup> Quædam de sanguinis different. in Morb. p. 15.

<sup>2</sup> The authors merely regard this as a confirmation of the law established by Andral and Gavarret, not as an original discovery.

The following table, extracted from their memoir, gives the mean results obtained from the analyses of blood in a number of cases of well marked inflammation.

	Males.	Females.
Density of defibrinated blood . . . .	1056·3	1054·5
Density of serum . . . . .	1027·0	1026·8
Water . . . . .	791·5	801·0
Solid constituents . . . . .	208·5	199·0
Fibrin . . . . .	5·8	5·7
Albumen . . . . .	66·0	65·8
Blood-corpuscles . . . . .	128·0	118·6
Extractive matters and salts . . . .	7·0	7·2
Fat . . . . .	1·742	1·669
Consisting of—Serolin . . . . .	0·020	0·024
Phosphorized fat . . . .	0·602	0·601
Cholesterin . . . . .	0·136	0·130
Saponified fat . . . .	0·984	0·914

The salts in 1000 parts of blood were :

Chloride of sodium . . . . .	3·1	3·0
Other soluble salts . . . . .	2·4	2·7
Phosphates . . . . .	0·448	0·344
Iron . . . . .	0·490	0·480

By a comparison of these results with the formulæ for healthy blood, (vide supra, p. 233,) we see that only three constituents, fibrin, cholesterin, and albumen, deviate from the normal standard. The first two of these constituents are increased, the last is diminished.]

#### I. PHLOGOSES OF THE CIRCULATING SYSTEM.

##### a. *Metrophlebitis puerperalis*.

In most of the cases of metrophlebitis puerperalis that have occurred in our lying-in institution as well as in the hospital, the blood exhibited all the symptoms of hyperinosis. According to Ebert's observations the clot was rather large, and so consistent that sections of it still displayed a powerful and well-marked tenacity. The surface, which was more or less concave, was either covered with a thin true buffy coat, or more frequently, with a rather thick, and often discoloured stratum of gelatinous substance, forming, what is termed, a false buffy coat. Gelatinous coagula, of a similar nature, were also frequently seen floating in the serum.

The microscope often detects pus in the blood, during the course of this disease. If, however, the quantity of pus is only small, its detection may be attended with much difficulty.<sup>1</sup> As the presence of pus in the blood has also been recognised in other pathological conditions, and many observations have recently been made upon the subject, I shall refer to this point more particularly when I speak of the presence of foreign substances in the blood.

I have analysed the blood of two women suffering from metrophlebitis puerperalis. The analyses gave :

	Analysis 15.	Analysis 16.
Water . . . . .	836.360	785.560
Solid residue . . . . .	163.640	214.440
Fibrin . . . . .	7.640	4.440
Fat . . . . .	3.120	4.320
Albumen . . . . .	103.358	112.770
Globulin . . . . .	40.000	74.130
Hæmatin . . . . .	2.080	3.440
Extractive matters and salts .	7.649	12.390
100 parts of hæmatoglobulin contained 5.0 of colouring matter.		100 parts of hæmatoglobulin contained 4.6 of colouring matter.

The blood in analysis 15 was taken from a woman aged 20 years, who was attacked in our lying-in institution with violent phlebitis uterina the day after her delivery. The pulse was full and hard, and 140 in the minute, previous to the bleeding. The post-mortem examination revealed a high degree of inflammation of the veins and of the uterus itself, with a copious deposition of pus.

In analysis 16, the blood was taken from a woman aged 20, who was seized fourteen days previously to the bleeding with a violent attack of phlebitis uterina, from which, however, she recovered by the use of venesection and mercury. Violent fever afterwards came on, accompanied by pain in the region of the uterus. The pulse was somewhat full and hard, and 132 in the minute. She died soon after, and the post-mortem examination proved the accuracy of the diagnosis.

[In a case of plegmasia alba dolens, accompanied with fever, occurring in a woman aged 21 years, six weeks after delivery,

<sup>1</sup> According to Gendrin, when there is pus in the blood, the serum deposits a viscid urinary-like sediment, or else is turbid and cloudy.



Becquerel and Rodier found a considerable diminution of the blood-corpuscles (92·6,) and an augmentation of the fibrin (4·2.) The cholesterin was in excess, (·223,) and the phosphates were abundant.]

*β. Carditis.*

Lecanu<sup>1</sup> analysed the blood of three men and five women, who were suffering from angiocarditis and endocarditis. Unfortunately he has made no observations on the physical characters of the blood, and the quantity of fibrin was also not ascertained. The analysis seems to have consisted simply in the separation of the clot from the serum, and then ascertaining the solid residue of each.

The blood of men gave the following results :

	Water.	Solid residue.	Residue of serum.	Blood-corpuscles.
1	821·02	178·98	77·59	101·39
2	880·48	119·52	77·62	41·90
3	807·27	192·73	96·35	96·38

The blood of women gave :

4	873·45	126·55	86·10	40·45
5	868·62	131·38	79·89	51·49
6	866·61	133·39	89·69	43·70
7	877·51	122·49	77·00	45·49
8	845·14	154·86	85·80	69·06
Healthy blood	790·00	210·00	80·00	130·00

It is much to be regretted that the fibrin was not determined in these researches, as the proportions of the solid residue, and especially of the corpuscles, indicate a high degree of hyperinosis.

Blood taken by repeated venesections from the same patient during carditis, differs in the following respect from blood similarly taken in cases of bronchitis, pneumonia, peritonitis, rheumatism, &c.; in these latter it becomes gradually poorer in solid constituents, and especially in corpuscles, while in the former, at least if we may judge from two analyses of Lecanu, the reverse takes place.

The man whose blood formed the object of the second analysis, on venesection being repeated 12 hours afterwards, yielded blood which left a solid residue of 139·1, and the woman from

<sup>1</sup> Etudes chimiques, etc., p. 110.

whom the blood in the eighth analysis was derived yielded, on a repetition of the venesection, blood which contained :

Water	. . .	841.62
Solid residue	. . .	158.38
Residue of serum	. . .	81.79
Blood-corpuscles	. . .	76.58

Lecanu noticed in the blood of one of these men a solid floating mass, (which, when dried, weighed about 100 grains.) It had a fleshy appearance, and on a section being made it exhibited a solid, loosely attached nucleus, of a brick-red colour, in the centre, which slowly dissolved in water. On the second occasion of this patient being bled, the clot presented even a more singular appearance. It was almost entirely formed of agglomerated clusters of small, round, white, grape-like masses, which were composed centrally of a bright red gelatinous substance.

[In a case of pericarditis with effusion, occurring in a woman aged 40 years, in which the blood was analysed by Becquerel and Rodier, the following results were obtained :

	1st Venesection.	2d Venesection.	3d Venesection.
Density of defibrinated blood	. 1045.8	1042.4	1045.5
Density of serum	. . 1023.0	1021.8	1024.3
Water	. . . 831.0		847.0
Solid constituents	. . . 169.0		153.0
Fibrin	. . . 2.3	2.3	3.4
Fat	. . . 1.094	1.094	
Albumen	. . . 53.0	51.0	60.4
Blood-corpuscles	. . . 105.0	92.0	78.0

In the first analysis the phosphates were in excess (0.684); in other respects the salts occurred in their normal proportions.

At the period of the third venesection, the heart-symptoms were much alleviated. The most remarkable feature in this blood is the extreme diminution of the albumen. There was no albumen in the urine.]

## II. INFLAMMATION OF THE RESPIRATORY ORGANS.

### a. *Bronchitis.*

The blood usually exhibits, at least when the symptoms are at all urgent, decided indications of hyperinosis. The buffy coat is scarcely ever absent, the serum is clear, and the clot

firm and consistent. The fibrin and fat are always more or less increased, and the hæmatoglobulin diminished.

	Analysis 17.	Analysis 18.
Water . . . .	797.500	757.831
Solid residue . . . .	202.500	242.269
Fibrin . . . .	4.320	
Fat . . . .	3.650	3.393
Albumen . . . .	96.890	109.080
Globulin . . . .	76.530	106.650
Hæmatin . . . .	3.200	8.762
Extractive matters and salts	11.560	14.500
100 parts of hæmatoglobulin contained 4.0 of colouring matter.		100 parts of hæmatoglobulin contained 8.4 of colouring matter.

In analysis 17 we observe, in a decided degree, the character of inflammatory blood, as far as regards the large quantities of fibrin and fat. The quantity of hæmatoglobulin, 79.73, is not so much diminished in proportion to the albumen in this case, as in those of phlebitis uterina.

The patient was a robust man, of about thirty years of age, who had only been suffering from the disease three days; pulse hard and very frequent. The blood of analysis 18 was taken from a child three years of age, by leeches, which is the reason why the fibrin was not determined.

Andral and Gavarret<sup>1</sup> have analysed the blood in six cases of bronchitis, and in all the instances in which fever was present, they found that well-marked character of inflamed blood, an increased quantity of fibrin. The maximum was 9.3, the minimum 5.7, in 1000 parts of blood.

I shall now give the results of their analyses.

Venesection.	Water.	Solid residue.	Fibrin.	Blood-corpuscles.	Solid portion of serum.	
1st Case {	1 763.3	236.7	7.3	148.8	80.6	
	2 793.6	206.4	9.3	110.2	86.9	
2d Case {	1 789.6	210.4	6.3	117.6	organic. 78.0	inorganic. 8.5
	2 769.5	230.5	5.9	139.6	76.7	8.3
3d Case {	1 782.2	217.8	5.9	129.4	76.3	6.2
	2 821.8	178.2	5.8	114.3	58.1	
4th Case {	1 800.2	199.8	6.0	131.3	62.5	
	2 808.1	191.9	7.1	125.5	59.3	
5th Case 1	808.3	191.7	5.7	98.2	87.8	
6th Case 1						
Healthy blood, according to Lecanu }	790.0	210.0	3.0	127.0	80.0	

<sup>1</sup> Annal. de Chim. et de Phys., vol. 75, p. 225.

The decreasing ratio of the corpuscles, and the increasing ratio of fibrin is less striking in this disease than in pneumonia and rheumatism. Andral and Gavarret give the following explanation of the first case, in which the high number 148·8 is assigned to the blood-corpuscles. This individual exhibited symptoms of typhoid fever at the period at which he was received into the hospital. In the second analysis the number is less by 38·6 than before. The symptoms of typhoid fever had now disappeared, and made way for those of bronchitis: the increase of fibrin from 7·3 to 9·3 sufficiently indicates the progress of inflammation.

In the fourth case the small quantity of solid constituents in the serum was coincident with a highly albuminous state of the urine; the patient, who was about 30 years of age, had for some time been in a weak and emaciated state. The urine in the fifth case, (a debilitated person 28 years of age, whose lower extremities were œdematous,) also contained albumen.

Andral and Gavarret have likewise analysed the blood in chronic bronchitis. They state that, as the febrile symptoms disappear, and the disease assumes the chronic form, the blood ceases to exhibit a large excess of fibrin, and in fact does not differ in any respect from ordinary healthy blood.

The same is the case if the chronic bronchitis is combined with pulmonary emphysema.

The average of five analyses made on the blood of four persons suffering in this way, scarcely differs from ordinary blood.

	Water.	Solid residue.	Fibrin.	Blood-corpuscles.	Solid portion of serum.
Mean of five analyses .	792·7	207·3	3·0	121·0	83·0
Healthy blood (Lecanu)	790·0	210·0	3·0	127·0	80·0

In one of these cases a second venesection was ordered, in consequence of the severity of the dyspnœa. The blood exhibited a diminution of 11 in the corpuscles, of ·6 in the fibrin, and of 22 in the solid constituents.

[Scherer has published an analysis of the blood of a woman in the seventh month of pregnancy, who was suffering from bronchitis, and probably from tubercular phthisis. The serum had a specific gravity of 1022·69, and contained in 1000 parts:

Water . . . .	911·516
Solid residue . . . .	88·484



The solid residue consisted of :

Albumen . . . .	77.978
Extractive matters . .	0.977
Salts . . . .	9.529

The whole blood contained, in 1000 parts :

Water . . . .	825.698
Solid residue . .	174.302
Fibrin . . . .	4.568
Albumen . . . .	70.636
Blood-corpuscles . .	71.069
Extractive matters . .	20.178(?)
Soluble salts . .	6.399
Earthy phosphates . .	1.825

The serum presented a singular milky appearance, arising from the presence of numerous minute granules in suspension. No fat-vesicles could be recognized by the microscope.

Becquerel and Rodier have analysed the blood in eight cases of acute bronchitis, four males and four females. The mean results are expressed in the following table :

	Males.	Females.
Density of defibrinated blood . .	1056.7	1056.6
Density of serum . . . .	1027.1	1027.7
Water . . . . .	793.7	803.4
Solid constituents . . . . .	206.3	196.6
Fibrin . . . . .	4.8	3.5
Fat . . . . .	1.621	1.715
Albumen . . . . .	64.9	68.8
Blood-corpuscles . . . . .	129.2	115.3
Extractive matters and salts . .	5.8	7.3

The salts consisted of :

Chloride of sodium . . . .	3.2	3.3
Other soluble salts . . . .	2.9	2.8
Phosphates . . . . .	0.346	0.309
Iron . . . . .	0.513	0.479.]

### *β. Pneumonia.*

The blood usually exhibits the characters of hyperinosis, more decidedly in pneumonia than in most other inflammatory diseases, it also retains its heat for a longer period.<sup>1</sup> The clot is rather below the ordinary size, very consistent, and does not

<sup>1</sup> Lauer found that blood, which, as it flowed from the vein, had a temperature of 97°·7, raised the thermometer to 83°·6 thirteen minutes after its removal from the body.

break down for a considerable time. It admits of being sliced, and the sections retain their consistency for some time. Its surface is covered with the buffy coat, and is more or less cupped. The serum is of a pure yellow colour. The quantity of solid constituents is usually less than in healthy blood.

The maximum of fibrin in my analyses was 9·15, which is the largest quantity that I have ever discovered in inflamed blood. The minimum was 3·4, and the mean of four analyses was 6·0. Andral and Gavarret found the maximum of fibrin to be 10·5; the minimum 4; and the mean to fluctuate between 7 and 8. They never met with more than 10·5 of fibrin in the whole course of their analyses.

The maximum of hæmatoglobulin, occurring in my researches, was 78, and the minimum 36, which is very far below the amount in healthy blood. Andral and Gavarret differ from me considerably on this point, (see my remarks on our comparative methods of analysis, page 241.) They make the maximum of the blood-corpuscles 137, and the minimum 83·7. We find, however, in the course of 58 analyses, made by them on the blood of 21 persons labouring under pneumonia, that the amount of corpuscles just reached the normal proportion in 5 cases, in 6 cases exceeded it, and in the 47 remaining cases fell below it. The average of these cases was 113, which is 14 below the normal quantity in healthy blood, according to Lecanu's analysis.

The maximum of fat, in my analysis, was 4·3, and the minimum (in a man aged 60 years) was ·7.

The maximum of solid residue was 202; the minimum was 160. In 51 out of the 58 analyses, made by Andral and Gavarret, the solid constituents exceeded the ordinary normal proportion.

In all these cases the quantity of the blood-corpuscles was very high: the fibrin, in two cases, reached 9·1; and in one case 9·0: in the others it was low, or amounted to only the mean of the fibrin in pneumonia.

The two highest amounts of solid residue found by Andral and Gavarret was 230, and 227; in these cases the maxima of corpuscles also occurred. The smallest amount of solid residue was 166, which corresponded with the minimum of blood-corpuscles. The mean quantity of solid residue, as deduced from

these 58 analyses, was 201, or 9 less than Lecanu's average for healthy blood.

I have made four analyses of the blood in pneumonia :

	Analysis 19.	Analysis 20.	Analysis 21.	Analysis 22.
Water . . .	839·848	798·500	803·179	803·400
Solid residue . . .	160·152	201·500	196·821	196·600
Fibrin . . .	9·152	6·020	5·632	3·443
Fat . . .	2·265	4·100	4·336	0·697
Albumen . . .	100·415	100·280	121·721	102·100
Globulin . . .	34·730	74·880	52·071	74·948
Hæmatin . . .	1·800	3·120	2·752	2·466
Extractive matters and salts . . .	8·003	10·500	10·309	11·258
100 parts of hæmatoglobulin contained . . .	4·9 of colouring matter.	4·0	5·2	3·2

The blood in analysis 19 was taken from a woman aged 40, who died a few days after the venesection. Dissections exhibited exudation, and tubercles in the lungs.

The blood in analysis 20 was taken from a vigorous man aged 30, who recovered; and in analysis 21, from a vigorous man aged 40, who also recovered.

The blood in analysis 22 was taken from a man 60 years of age, who suffered from cough, thoracic oppression, &c., and whose pulse was hard and full. I am ignorant of the result in this case.

The following are the maxima, minima, and average results, obtained by Andral and Gavarret :

	Water.	Solid residue.	Fibrin.	Corpuscles.	Solid residue of serum.
Maximum . . .	834·4	229·5	10·5	137·8	95·2
Minimum . . .	770·5	165·6	4·0	83·2	66·7
Average . . .	799·0	201·0	7·3	114·1	81·0

The following table indicates the differences that are found in pneumonic blood during repeated bleedings. It is drawn up by Andral and Gavarret,<sup>1</sup> and corresponds generally with the table already given for the blood taken in a similar manner during bronchitis. It is, however, entirely at variance with Lecanu's statement regarding the blood in carditis. (See page 254.)

<sup>1</sup> Annales de Chimie et de Physique, vol. 75, p. 254.

	Venesection.	Day of disease.	Water.	Solid residue.	Fibrin.	Corpuscles.	Solid residue of serum.
1st Case	1	2	818.0	182.0	4.0	111.3	66.7
	2	3	818.5	181.5	5.5	107.7	68.3
	3	5	820.9	179.1	6.5	101.1	71.5
	4	7	834.4	165.6	9.0	83.2	73.4
2d Case	1	3	773.0	227.0	5.2	137.8	84.0
	2	4	782.3	217.7	7.3	125.5	84.9
	3	5	795.0	205.0	6.9	117.4	80.7
	4	6	800.4	199.6	8.0	111.5	80.6
3d Case	1	4	781.5	218.5	5.5	129.8	83.2
	2	5	788.3	211.7	6.8	116.3	88.6
	3	9	823.9	176.1	6.4	95.7	74.0

This table is sufficient to show that the blood taken from the same individual in different consecutive bleedings varies considerably. The blood taken at the later bleedings contains less solid constituents, less blood-corpuscles, more fibrin, and more solid residue of serum<sup>1</sup> than the blood which is taken earlier.

This statement is, however, only true within certain limits; if the bleedings are carried beyond a certain extent, the fibrin, as well as the corpuscles, are diminished; the whole quantity of solid residue becomes less, whilst the residue of the serum increases. In the third case this proportion is seen on comparing the blood taken on the third, with that taken on the second bleeding; but it is much more strikingly shown in the analyses made by Andral and Gavarret, of the blood in acute rheumatism, as will be seen by the following numerical data.<sup>2</sup>

Bleeding.	Day of Disease.	Water.	Solid residue.	Fibrin.	Blood-corpuscles.	Solid residue of serum.
1	8	778.8	221.2	6.1	123.1	92.0
2	9	780.9	219.1	7.2	120.7	91.2
3	10	788.0	212.0	7.8	112.8	91.4
4	13	799.0	201.0	10.2	101.0	89.8
5	17	813.9	186.1	9.0	89.2	87.9
6	28	826.2	173.8	7.0	83.3	83.0

My own observations regarding the blood taken by repeated venesections during peritonitis, give perfectly similar results. I shall endeavour to give an explanation of the origin of these changes at the end of the section on hyperinosis.

Dr. J. Davy<sup>3</sup> has instituted numerous researches on the

<sup>1</sup> [This conclusion is not very obvious.]

<sup>2</sup> Op. cit. p. 246.

<sup>3</sup> Edinb. Med. and Surg. Journal, 1839.



blood found in the body after death : in a case of pneumonia, he found a large quantity of fluid blood, clot, and fibrous coagula in the heart. The fluid portion did not coagulate after exposure to the air for 24 hours. In another instance, the fluid portion when exposed to the air, coagulated rapidly and formed a buffy coat.

[Dr. Rindskopf<sup>1</sup> has published several analyses of the blood in pneumonia.

1. A young man, with a very severe attack of pneumonia : delirium, and all the signs of arachnitis. After death, a considerable effusion of pus was found on the membranes of the brain. Two venesections were instituted during the last thirty-six hours. The first gave fibrin 5·470. The second analysis was more perfect, and yielded :

Water . . . . .	828·566
Solid constituents . . . . .	171·434
Fibrin . . . . .	6·674
Albumen and blood-corpuscles . . . . .	150·103
soluble salts . . . . .	8·302
Insoluble salts . . . . .	1·107
Extractive matters . . . . .	5·248

2. A man, aged 60 years, who had suffered for a considerable period from chronic bronchitis and emphysema, was attacked with broncho-pneumonia. The blood was taken shortly before his death, and contained, in 1000 parts :

Water . . . . .	812·566
Solid constituents . . . . .	187·434
Fibrin . . . . .	12·726
Albumen and blood-corpuscles . . . . .	160·300
Salts . . . . .	10·930
Extractive matters . . . . .	3·478

3. In the blood of a young man, aged 19 years, suffering from pneumonia, Rindskopf found :

	1st Venesection.	2d Venesection.
Water . . . . .	775·448	783·944
Solid constituents . . . . .	224·552	216·056
Fibrin . . . . .	6·702	7·723
Albumen . . . . .	79·021	65·744
Blood-corpuscles . . . . .	122·097	120·682
Salts . . . . .	9·201	10·416
Extractive matters . . . . .	7·531	11·661

<sup>1</sup> Ueber einige Zustände des Blutes.

4. In a case of pneumonia after catarrh, four analyses were made, the blood taken at the first venesection apparently not having been examined. In addition to the bleedings, tartarized antimony and calomel were administered: recovery.

	2d Venes.	3d Venes.	4th Venes.	5th Venes.
Water . . . .	796.494	793.362	807.699	809.650
Solid constituents . .	203.506	206.638	192.301	190.350
Fibrin . . . .	5.919	7.715	10.384	8.155
Albumen and blood-corpuscles	173.605	169.883	165.960	160.522
Soluble salts . . .	10.188	7.952	} 15.957	11.531
Insoluble salts . .	1.340	1.404		4.151
Extractive matters . .	11.454	19.684		5.991

5. In a case of pneumonia of four weeks' standing, accompanied with catarrh and delirium tremens, in which tartar emetic was administered, and recovery took place, the following results were obtained:

	2d Venesection.	3d Venesection.	4th Venesection.
Water . . . .	793.237	797.915	
Solid constituents . .	206.763	202.085	
Fibrin . . . .	7.893	9.087	9.478
Albumen and corpuscles	157.916	164.451	
Salts . . . .	10.978	8.291	
Extractive matters . .	29.975	20.256	

Heller<sup>1</sup> has analysed the blood of a powerful young man, aged 21 years, suffering from pneumonia, the left lung being perfectly hepatized.

The colour of the blood was rather dark. As it flowed from the vein, its reaction was perfectly neutral. The serum, after the separation of the clot, had an alkaline reaction, a specific gravity of 1.025, and was of a darker yellow colour than usual, although the addition of nitric acid disproved the presence of biliphæin. The blood was composed of 600 parts of clot and 400 of serum. It contained, in 1000 parts:

Water . . . .	773.266
Solid constituents . .	226.744
Fibrin . . . .	4.320
Blood-corpuscles . .	145.574
Residue of serum . .	76.850

Becquerel and Rodier have analysed the blood of five women

<sup>1</sup> Archiv für physiologische und pathologische Chemie und Mikroskopie. Wien, 1844, vol. 1, p. 3.

suffering from pneumonia, two of whom were bled only once, while in three venesection was repeated.

The mean composition of the blood is expressed in the following table:

	1st Venesection.	2d Venesection.
Density of defibrinated blood . . . . .	1052·6	1050·2
Density of serum . . . . .	1025·0	1025·0
Water . . . . .	801·0	808·0
Solid constituents . . . . .	199·0	192·0
Fibrin . . . . .	7·4	6·3
Fat . . . . .	1·687	1·618
Albumen . . . . .	61·1	59·7
Blood-corpuscles . . . . .	122·5	113·9
Extractive matters and salts . . . . .	6·4	7·4

The following salts were contained in 1000 parts of blood:

Chloride of sodium . . . . .	2·8	3·1
Other soluble salts . . . . .	2·7	2·4
Phosphates . . . . .	0·308	0·445
Iron . . . . .	0·493	0·512

Zimmerman<sup>1</sup> has found the specific gravity of the blood in this disease as high as 1065.

The following ultimate analyses of dried pneumonic blood have been recently published:<sup>2</sup>

	Ash.	C.	H.
Blood buffed, 1st Venesection . . . . .	4·365	57·428	8·615
„ 2d ditto . . . . .	4·081	52·280	—
„ 1st ditto . . . . .	3·880	51·966	8·543
„ 2d ditto . . . . .	3·784	51·149	7·832

Two analyses of the blood in cases of pneumonia biliosa have recently appeared, one by Scherer, the other by Heller.

The individual whose blood was analysed by Scherer was a robust young man, aged 29 years.

The clot was tolerably firm and tough, and covered with a greenish yellow buffy coat. The serum exhibited a similar tint, and nitric acid indicated the existence of biliphæin in the urine. The conjunctiva was coloured yellow, and there was considerable gastric disturbance.

<sup>1</sup> Hufeland's Journal, 1843.

<sup>2</sup> Hoffmann, *Annalen der Chemie und Pharmacie*, April 1844. According to Macaire and Marceet (*Mem. de la Société Phys. et d'Hist. Nat. de Genev.*, vol. 5, p. 223) healthy venous blood contains C 55·7, H 6·4, N 16·2, and O 21·7.

The blood drawn at the first venesection yielded :

Water	. . . .	779.00
Solid constituents	. . . .	221.00
Fibrin	. . . .	9.70
Blood-corpuscles	. . . .	124.60
Albumen	. . . .	72.26
Salts	. . . .	9.57
Extractive matters	. . . .	4.83

Blood was again taken, in consequence of further symptoms of congestion. It yielded :

Water	. . . .	785.00
Solid constituents	. . . .	215.00
Fibrin	. . . .	9.40
Blood-corpuscles	. . . .	122.26
Albumen	. . . .	65.36
Salts	. . . .	8.31
Extractive matters	. . . .	9.67

Three days after this venesection the patient was again bled. The blood contained :

Water	. . . .	780.00
Solid constituents	. . . .	220.00
Fibrin	. . . .	12.72
Blood-corpuscles	. . . .	118.47
Albumen	. . . .	69.83
Salts	. . . .	7.63
Extractive matters	. . . .	11.35

The blood obtained by a fourth venesection contained :

Water	. . . .	796.00
Solid constituents	. . . .	204.00
Fibrin	. . . .	8.87
Blood-corpuscles	. . . .	106.26

In Heller's case the blood was taken from a robust man, aged 31 years. The clot was firm, and slightly buffed; the serum was of a deep yellowish-red colour, very alkaline, of specific gravity 1023, and, on the addition of nitric acid, a blue coagulum was formed, indicative of the presence of biliphæin.

The blood consisted of 521 parts of clot and 479 of serum. It contained, in 1000 parts :



Water	.	.	.	.	.	781·659
Solid residue	.	.	.	.	.	218·351
Fibrin	.	.	.	.	.	6·113
Blood-corpuscles	.	.	.	.	.	147·114
Residue of serum (with biliphæin)						65·124

Heller observes that he has often been able to detect biliphæin in the blood of pneumonic patients when there have been no other indications of a disordered state of the hepatic functions.

In pneumonia venosa the buffy coat is absent. (Schönlein.)]

### *γ. Pleuritis.*

Never having analysed pleuritic blood, I shall merely give the results obtained by Andral and Gavarret.

That the blood in this disease may exhibit considerable differences, will be seen by the following cases.

1st stage. Pleuritis in its early stage, before any effusion has occurred. In two cases of this nature, Andral and Gavarret found the quantity of fibrin increased to 5·8 and 5·9.

2d stage. Pleuritis not yet advanced, but effusion.

Andral and Gavarret found that the quantity of fibrin varied from 4 to 6 in eight cases of this nature.

3d stage. Pleuritic effusion of some duration ; no fever. In four cases of this nature, in which effusion had occurred during well-marked pleuritis, from two to four months previously, the quantity of fibrin was increased, less certainly than in the preceding cases, but still in one instance rising as high as 4·8, and averaging about 4.

Hence it follows that the fibrin is increased in the blood in pleuritis, especially in the acute form, accompanied with fever ; the increase, however, is not so decided as in pneumonia, bronchitis, and (as we shall presently see) in acute rheumatism.

Nasse<sup>1</sup> states that the buffy coat is particularly characteristic, and seldom absent in pleuritic blood.<sup>2</sup>

<sup>1</sup> Das Blut, etc., p. 61.

<sup>2</sup> The buffy coat was absent 9 times in 35 cases in which blood was extracted during pleuritis, 3 times in 11 cases of pneumonia, and twice in 5 cases of bronchitis.

Andral and Gavarret's analyses gave the following results.

	Venesection.	Water.	Solid residue.	Fibrin.	Blood-corpuscles.	Solid residue of serum.
1st Case	1	774.2	225.8	5.9	127.7	92.2
2d	" 1	789.4	210.6	5.4	90.4	114.8
3d	" 1	845.6	154.4	5.0	68.3	81.1
4th	" 1	782.0	218.0	5.2	122.9	89.9
5th	" 1	815.0	185.0	5.0	91.5	88.9
6th	" { 1	802.6	197.4	5.0	107.4	85.0
	" { 2	807.6	192.4	5.0	102.5	84.9
7th	" 1	833.1	166.9	4.1	84.7	78.1
8th	" 1	763.3	236.7	4.9	141.1	90.7
9th	" 1	861.3	198.7	4.8	120.8	73.1
10th	" { 1	783.5	216.5	3.9	128.8	83.8
	" { 1	780.3	219.7	5.8	118.9	95.0
11th	" 1	816.9	183.1	3.8	92.8	86.5
12th	" { 1	783.0	217.0	3.5	135.4	78.1
	" { 2	798.5	201.5	4.2	124.2	73.1
Healthy blood		790.0	210.0	3.0	127.0	80.0

Lauer<sup>1</sup> states that he has found the serum turbid in pleuritis.

Caventou<sup>2</sup> analysed the blood in a case of chronic pleuritis, accompanied with vertigo. It was turbid, of a dirty-red colour, and covered with a soft light-coloured buffy coat. The clot was moderately large, and floated in a yellowish-white, milky serum, which was perfectly neutral, devoid of smell or taste, coagulable by heat, but not by acids or alcohol, and scarcely at all by corrosive sublimate.

[Becquerel and Rodier have analysed the blood of five men attacked with uncomplicated and acute pleuritis. The mean composition of the blood is given in the following table.

Density of defibrinated blood	. . . . .	1055.0
Density of serum	. . . . .	1026.0
Water	. . . . .	798.6
Solid constituents	. . . . .	201.4
Fibrin	. . . . .	6.1
Fat	. . . . .	1.905
Albumen	. . . . .	65.4
Blood-corpuscles	. . . . .	120.4
Extractive matters and salts	. . . . .	7.6

The salts consisted of:

Chloride of sodium	. . . . .	3.0
Other soluble salts	. . . . .	2.0
Phosphates	. . . . .	0.478
Iron	. . . . .	0.461

<sup>1</sup> Quædam de Sanguine diff., etc.

<sup>2</sup> Annal. de Chim. et de Phys. vol. 39, p. 288.

The blood-corpuscles and the albumen are considerably diminished while the fibrin is increased.]

### III. INFLAMMATION OF THE CHYLOPOIETIC VISCERA.

#### a. *Angina tonsillaris (amygdalitis).*

Andral and Gavarret analysed the blood of four persons suffering from angina vera, and they always found, in a greater or less degree, the distinctive characters of hyperinosis. They obtained the following results.

Venesection.	Day of disease.	Water.	Solid residue.	Fibrin.	Blood-corpuscles.	Solid residue of serum.
1st Case { 1	4	782·6	217·4	6·1	111·0	100·3
{ 2	5	793·6	206·4	7·2	105·3	93·9
2d    "    1	6	777·9	222·1	5·4	126·0	90·7
3d    "    { 1	2	819·5	180·5	4·4	90·0	88·1
{ 2	3	830·2	169·8	6·4	79·5	83·9
4th   "    1	—	779·6	220·4	3·8	120·3	96·3
Healthy blood		790·0	210·0	3·0	127·0	80·0

With the exception of the 4th case, which was one of chronic angina, and in which the blood presents no striking deviations from the healthy standard, and of the 2d case, in which the blood is extremely rich in solid constituents, the remainder exhibit a decided decrease in the quantity of the corpuscles<sup>1</sup>, and a less marked increase of fiction.

#### β. *Hepatitis and lienitis.*

Accurate quantitative analyses of the blood in these inflammatory diseases are still wanted. It has been frequently observed that the proportion of fat is considerably increased in the blood during hepatitis, and Trail has found the serum milky on several occasions; Nasse<sup>2</sup> has occasionally seen it so highly coloured with biliphæin as immediately to tinge paper on being dipped in it; and Lauer<sup>3</sup> has observed that a yellow-coloured sediment is deposited by the serum upon the buffy coat, during this disease.

<sup>1</sup> In the blood obtained by the second venesection in Case 3, they fall even below the solid residue of the serum. Andral and Gavarret, however, attribute the low amount of corpuscles in this instance to the circumstance of the patient having been for some time under the poisonous influence of lead.

<sup>2</sup> Das Blut, etc., p. 78.

<sup>3</sup> Quædam de Sanguinis different. in Morbis, p. 34.

In the milky serum to which we have adverted, Trail<sup>1</sup> found 21·1% of solid constituents, which were composed of fatty oil 4·5, albumen 15·7, soluble matter ·9. The water amounted to 78·9%. The specific gravity of the serum was 1·087; it was of a creamy consistence, and became thinner when exposed to a gentle warmth; when left to itself, even for weeks, it did not deposit any sediment.

In another instance the specific gravity was 1·025, and the solid constituents amounted to 15·2%, of which a considerable portion was oil.

The serum has been observed by Cullen, Testa, and Heusinger to be turbid in lienitis (Nasse).

### γ. *Peritonitis.*

The blood in peritonitis, and especially in the form denominated puerperal fever, exhibits in a tolerably well marked degree the characters of hyperinosis. I made two analyses of the blood of a patient suffering from peritonitis puerperalis, and found that the fibrin amounted to twice as much as in healthy blood. Andral and Gavarret obtained similar results.

My analyses yielded :

	Analysis 23.	Analysis 24.
Water . . . .	784·941	787·064
Solid residue . . .	215·059	212·936
Fibrin . . . .	4·459	4·366
Fat . . . .	4·035	3·350
Albumen . . . .	107·406	109·714
Globulin . . . .	84·623	83·532
Hæmatin . . . .	3·591	3·733
Extractive matters and salts	10·350	9·440
The hæmatoglobulin contained 4·0% of colouring matter.		The hæmatoglobulin contained 4·2% of colouring matter.

The blood in these analyses were taken from a woman aged 33 years, who, according to Dr. Ebert's report, exhibited the first symptoms of peritonitis on the evening of the second day after her confinement.

The belly was somewhat swelled, and tender to the touch. There was extreme heat, violent thirst, and rapid respiration. The pulse was quick, hard, and full, 130 in the minute. The blood formed a tolerably firm clot, and was covered with a buffy coat of a line and a half thick. There was violent exacerbation

<sup>1</sup> Edinb. Med. and Surg. Journal, vol. 17.



on the evening of the third day: the countenance was much flushed, there was delirium, the pulse was 140, and hard. It was at this period that the blood referred to in analysis 23 was taken.

On the fourth day the abdomen was tympanitic: the head-symptoms were comparatively gone: the countenance was pale, pulse 140, soft and small. The composition of the blood now taken is given in analysis 24. The patient died. Dissection showed that the thoracic organs were healthy, but that there was exudation in the abdomen, with flocculent and purulent matter: the same was found in the uterus and intestines. The vessels on the peritoneal surface were fully injected; and on cutting into the uterus, milky pus was observed to exude in pearly drops from the distended lymphatic vessels.

In relation to the chemical constitution of the blood taken at the second venesection, we may observe (*vide supra*, p. 261) that there is a diminution not only of the quantity of the solid constituents, but also of the hæmatoglobulin or blood-corpuscles. The fibrin, however, instead of being increased, is diminished by .01, which may probably be accounted for by the circumstance of the pulse not having increased in frequency, and having even become less hard.

Andral and Gavarret<sup>1</sup> have made eight analyses of the blood of four persons suffering from peritonitis: one was a case of simple peritonitis; the others were instances of metroperitonitis. Two of the cases terminated fatally, and in these a large quantity of pus was found in the abdominal cavity.

Their analyses gave the following results:

	Venesection.	Water.	Solid residue.	Fibrin.	Blood-corpuscles.	Solid residue of serum.
1st Case	1	787.2	212.8	5.5	122.8	84.5
2d "	{ 1	822.9	177.1	5.4	88.3	83.4
	{ 2	831.6	168.4	5.3	73.6	89.5
	{ 3	851.0	149.0	3.6	60.5	84.9
3d "	1	786.4	213.6	7.2	117.0	89.4
4th "	{ 1	789.4	210.6	3.8	120.0	86.8
	{ 2	802.7	197.3	4.7	109.5	83.1
	{ 3	813.5	186.5	6.1	100.3	80.1
Healthy blood		790.0	210.0	3.0	127.0	80.0

Andral and Gavarret make the following observations on these analyses. Two of them exhibited a considerable decrease<sup>2</sup>

<sup>1</sup> Annal. de Chimie et de Physique, vol. 75, p. 261.

<sup>2</sup> They do not, of course, refer to an absolute decrease below the healthy standard, but merely below the ordinary standard of the blood in inflammatory disorders.

in the quantity of fibrin. In one of these cases (the third venesection of the second case) it amounted only to 3·6 in 1000 parts of blood. The blood for this analysis was taken at a period when the patient was much reduced by marasmus.

Dissection revealed the existence of pus in the cavity of the abdomen, a consequence of the previous inflammation.

The second instance is that of the 1st venesection of the fourth case, in which 3·8 of fibrin were found. This case was that of a woman labouring under suppression of the catamenia, who was seized with violent pains in the abdomen, which were attributed to mere uterine congestion: there was no fever present. The blood contained 3·8 of fibrin, little more than the normal proportion. At the expiration of two days the pain became more acute, and the blood taken at the second venesection contained 4·6 of fibrin. From this rapid increase of the fibrin it was inferred (although there was no fever) that something more than simple hyperæmia of the uterus was present; and, in point of fact, on the following day all the symptoms of metropéritonitis were established.

At the third venesection, 6·1 of fibrin were found in the blood. After this time the patient began to improve.

This case is of much interest, as affording an illustration of the importance of chemical research in the formation and establishment of diagnosis.

[A singular case of peritonitis, in which milky serum was observed, has been recently published by Heller. It occurred in a robust but not corpulent man, aged 40 years. The blood, when first drawn, was of the ordinary colour, and on standing, the clot and serum separated perfectly, the former not exhibiting a buffy coat.

In 1000 parts of blood there were :

Fibrin . . . .	4·72
Blood-corpuscles . .	80·13

In 1000 parts of the serum there were :

Water . . . .	829·515
Solid residue . . .	170·485
Fat . . . .	50·473
Albumen . . . .	108·791
Extractive matters and salts	11·221

The fat was perfectly saponifiable with potash, and yielded no traces of cholesterin.

After the separation of the clot, the serum exactly resembled milk : its reaction was alkaline, and its specific gravity 1024·35.

In the blood of a girl, aged 18 years, suffering from a slight attack of peritonitis, Becquerel and Rodier found a marked diminution of the blood-corpuscles, and an increase of the fibrin (5) ; the albumen remained normal, the phosphates and the cholesterin were increased.

The serum was abundant, limpid, and yellow ; the clot large and firm.

In a woman, aged 24 years, attacked with metroperitonitis, Scherer observed a tolerably large buffy coat, apparently more gelatinous than tough. The clot was rather large, but not very firm. The serum was neutral.

The blood contained in 1000 parts :

Water	. . . .	814·53
Solid constituents	. .	185·47
Fibrin	. . . .	5·32
Albumen	. . . .	96·35
Blood-corpuscles	. .	70·16
Fat and extractive matters	. .	6·02
Salts	. . . .	7·13

Two days afterwards the blood contained :

Water	. . . .	832·58
Solid constituents	. .	167·42
Fibrin	. . . .	4·02
Albumen	. . . .	100·25
Blood-corpuscles	. .	52·30
Salts and extractive matters	. .	11·42

The buffy coat had a more gelatinous appearance, and the serum was redder than on the former occasion. Death occurred two days after the second venesection.

In a case of metroperitonitis, in which the blood was analysed by Heller, the clot was soft, and exhibited a well-marked buffy coat. The serum was clear, but of a deep yellow colour, and contained a large quantity of biliphæin. Its specific gravity was 1024. The blood consisted of 486·5 parts of clot and 513·5 of serum, and contained :

Water	. . . . .	820.02
Solid constituents	. . . . .	179.98
Fibrin	. . . . .	7.78
Blood-corpuscles	. . . . .	87.12
Residue of serum (with biliphæin)	. . . . .	85.08]

## IV. INFLAMMATION OF THE UROPOIETIC VISCERA.

*Nephritis and cystitis.*

Very little has been done in the chemistry of the blood in these diseases.

Lauer<sup>1</sup> found that the blood taken from a man suffering from nephritis, and who speedily fell a victim to the disease, strongly resembled milk.

Andral and Gavarret<sup>2</sup> analysed the blood of a man suffering from inflammation of the bladder, and found it to be composed of

Water	. . . . .	785.8
Fibrin	. . . . .	5.4
Blood-corpuscles	. . . . .	111.4
Solid residue of serum	. . . . .	97.4

The increase of the fibrin and the diminution of the corpuscles show that this blood is similar in its constitution to the blood in other inflammatory diseases.

The blood in acute rheumatism, erysipelas, tubercular phthisis, puerperal mania, &c., is so strongly impressed with the ordinary characters of hyperinosis, that we shall consider it, in reference to those diseases, in the present place.

*a. Rheumatismus acutus.*

In acute rheumatism, accompanied by fever, the blood always exhibits, in a more or less marked degree, the characters of hyperinosis.

The clot is rather small, consistent,<sup>3</sup> and sometimes covered

<sup>1</sup> Op. cit. p. 32.

<sup>2</sup> Op. cit. p. 266.

<sup>3</sup> Nasse states that, in inflammatory rheumatism, he has observed a solid clot, although, when the buffy coat was very strong, its consistence was less on its lower surface. According to Haller, a thick clot is formed in acute rheumatism. (Stark, Allg. Patholog. p. 950.) Jennings, on the other hand, maintains that the clot under the buffy coat is so loose as to fall to pieces on the slightest touch. (Course of Lectures on the Physiology and Pathology of the Blood, by Ancell. 'The Lancet,' 1840, p. 841.)



with a strong buffy coat, The serum is usually clear, and of a deep yellow colour.

I have made only one analysis of the blood in acute rheumatism accompanied with fever. I found that the quantity of fibrin was considerable, that the quantity of fat was sensibly increased, and of hæmatoglobulin much diminished in relation to the normal proportions.

Andral and Gavarret have analysed the blood in 14 cases of acute rheumatism. They found that if the blood was taken during the period of acute pain and fever, the fibrin existed in much larger proportion than in normal blood.

On the other hand, they found that the quantity of fibrin was even less than in normal blood, in the case of an individual who was bled after the subsidence of the pain and of the fever.

In those cases in which the pain and fever returned, after an improvement had taken place, an increase of fibrin was again observed.

My analysis gave the following results :

Analysis 25.

Water	.	.	.	.	801.500
Solid residue	.	.	.	.	198.500
Fibrin	.	.	.	.	6.320
Fat	.	.	.	.	3.150
Albumen	.	.	.	.	100.540
Globulin	.	.	.	.	71.560
Hæmatin	.	.	.	.	3.000
Extractive matters and salts					11.860

The blood was taken from a man aged 35 years, in whom the joints of the foot and knee were much swollen and very painful : the joints of the hand were less swollen, but very tender on being touched. The febrile symptoms were not severe.

The following table exhibits the maxima, minima, and mean of 43 analyses made by Andral and Gavarret upon the blood of 14 individuals suffering from acute rheumatism :

	Water.	Solid residue.	Fibrin.	Blood-corpuscles.	Residue of serum.
Maxima	839.6	228.4	10.2	130.0	104.8
Minima	771.6	160.4	2.8	70.1	76.9
Mean	805.4	194.6	6.7	101.0	86.0
Healthy blood.	790.0	210.0	3.0	127.0	80.0

100 parts of the solid residue of the serum gave, on an average, 7.9 of inorganic constituents.

The quantity of blood-corpuscles only once exceeded the quantity in normal blood, and this instance coincides with that in which the solid constituents generally attained their maximum, 228·0: in most instances it was considerably diminished, and hence we find that the average displays the corpuscles 16 below the ordinary proportion. In only four cases was the quantity of fibrin lower than 5·0. Andral and Gavarret remark that the acuteness of the pain seems to have a greater influence on the increase of the fibrin than the stage or duration of the disease. The blood will be found to contain as large a proportion of fibrin at the commencement of a rheumatic attack which begins very severely, as at a much later period in a case commencing mildly, but in which acute pain gradually supervenes. This will be seen by the following analyses:

	Venesection.	Day of disease.	Water.	Fibrin.	Blood-corpuscles.	Residue of serum.
1st Case	1	4	797·1	8·9	109·3	84·7
	2	5	796·9	9·8	107·5	81·8
	3	6	812·5	8·5	95·4	83·6
	4	10	820·6	6·4	93·5	79·5
	5	25	789·7	2·8	117·9	89·6
2d Case	1	8	778·8	6·1	123·1	92·0
	2	9	780·9	7·2	120·7	91·2
	3	10	788·0	7·8	112·8	91·4
	4	13	799·0	10·2	101·0	89·8
	5	17	813·9	9·0	89·2	87·9
	6	28	826·2	7·0	83·8	83·0

In the first case, the maximum of fibrin is found in the blood taken at the second venesection, and as early as the fifth day of the disease. In the second case, on the contrary, it did not occur until the fourth venesection, upon the thirteenth day of the disease, when nearly all the joints were reported to be in a swollen and painful state. These symptoms began to diminish after the next two bleedings; the fever, however, still continued.

The minimum of fibrin in the first case occurred at the period of the fifth venesection, and is even less than the amount in normal blood: the corpuscles are now considerably increased. This venesection was performed on the eighteenth day of convalescence, after all pain had entirely disappeared, and after the patient had been put upon a nourishing diet.

Andral and Gavarret show in the following table how the remission of the fever influences the quantity of fibrin.

Venesection.	Day since commencement of disease.	Water.	Fibrin.	Blood-corpuscles.	Residue of serum.
1	4	795·0	6·2	111·9	86·9
2	19	801·5	3·7	102·0	82·8
3	24	814·9	5·5	95·8	83·9
4	34	833·8	5·8	81·5	78·9

The second bleeding was ordered when the fever had completely gone, and only a few slight pains remained; the third upon the occurrence of a relapse; and the fourth during a continuation of the pain and fever.

[Dr. Rindskopf has analysed the blood of a woman suffering from rheumatism, accompanied with pneumonia. He found in 1000 parts:

	1st Venesection.	2d Venesection.
Water . . . . .	809·973	
Solid constituents . . . . .	190·027	
Fibrin . . . . .	4·652	5·856
Matters coagulable by heat . . . . .	166·954	
Salts . . . . .	12·188	
Extractive matters . . . . .	6·233	

Becquerel and Rodier have analysed the blood of four men suffering from acute rheumatism. The mean composition of the blood is given in the following table:

Density of defibrinated blood . . . . .	1055·5
Density of serum . . . . .	1025·8
Water . . . . .	798·9
Solid constituents . . . . .	101·1
Fibrin . . . . .	5·8
Fat . . . . .	1·647
Albumen . . . . .	66·9
Blood-corpuscles . . . . .	118·7
Extractive matters and salts . . . . .	8·1 ]

Andral and Gavarret have analysed the blood of ten individuals suffering from chronic and subacute articular rheumatism. No peculiarly striking results were obtained. The proportion of fibrin in no instance exceeded 5·0, and in two cases was as low as 2·9 and 2·6. The blood-corpuscles in one instance amounted to no less than 154·3, and the solid constituents to 259·1. In the other cases the corpuscles were below the healthy average.

These results lead us to the conclusion that, provided there

are no other disturbing influences, as the rheumatism loses its acute character, the blood gradually throws off the specific characteristics of hyperinosis.

The following table exhibits the maxima, minima, and mean results, as deduced from 10 analyses :

	Water.	Solid residue.	Fibrin.	Blood-corpuscles.	Solid residue of serum.
Maximum .	826·8	259·9	5·1	154·3	102·0
Minimum .	741·1	173·2	2·6	79·0	77·1
Mean .	782·7	217·3	3·8	108·2	95·2
Healthy blood .	790·0	210·0	3·0	127·0	80·0

I add the results of some of the analyses, on account of the interesting remarks that Andral and Gavarret have made on them.

	Water.	Solid residue.	Fibrin.	Blood-corpuscles.	Solid residue of serum.
1	826·8	173·2	4·8	79·0	89·4
2	818·3	181·7	4·6	89·1	88·0
3	815·4	184·6	4·0	82·6	98·0
4	741·1	259·9	2·6	154·3	102·0

The blood in the first of these cases was taken from a colour-mixer under the influence of lead, to which circumstance Andral and Gavarret attribute the deficiency of the corpuscles. In the second of these cases, the blood was taken from a person who had suffered from an acute attack of rheumatism, for which he had been bled six times (!), besides having had 200 leeches (!) applied; a fully sufficient reason why the blood contained only 89·0 of corpuscles. The blood in the third analysis was taken from a person suffering from incipient chlorosis. In the fourth case the blood was taken from a vigorous person, 20 years of age, which accounts for the unusually large quantity of corpuscles, as well as of solid constituents generally.

### *β. Erysipelas.*

I have not made any analyses of the blood in erysipelas. Andral and Gavarret found that the blood, in ordinary erysipelas attended with fever, was so rich in fibrin, and the quantity of corpuscles so reduced, as to leave no doubt of the existence of hyperinosis.

It is by no means easy to detect the peculiar properties of the blood depending on this disease, for as soon as any inflammatory fever is complicated with it, the blood will, from that cause alone, assume a state of hyperinosis. Moreover, the mere



circumstances of temperament, age, &c. may induce a state of the blood partially approximating to hyperinosis, or to hypinosis. Contradictory results may also arise from variations in treatment, as far as venesection is concerned. We know, for instance, that in France the lancet is used with an unsparing hand; and if venesection be ordered in a case of erysipelas in which no serious inflammatory affection is present, it is by no means impossible that the blood may exhibit the character of hypinosis. In Germany, on the contrary, venesection is seldom prescribed unless decided inflammatory symptoms present themselves; in this case the blood is sure to exhibit the characters of hyperinosis. Schönlein states that in erysipelas the serum is always tinged yellow by the colouring matter of the bile; that the proportion of the serum to the clot is large; and that the consistence of the clot is inversely as its size. These characters decidedly indicate a state of hyperinosis.

Andral and Gavarret have made eight analyses of the blood of five persons, four of whom were suffering from erysipelas of the face, and one from inflammatory erysipelas of the foot. In seven of these cases the fibrin was materially increased; in three instances it amounted to 5·0, in three to 6·0, and in one to 7·0. In a much shorter and milder case, in which there was but little fever, it amounted to only 3·6.

Their analyses gave the following results:

Venesection.	Day since commencement of disease.	Water.	Solid residue.	Fibrin.	Blood-corpuscles.	Solid residue of serum.		
						<i>organic.</i>	<i>inorganic.</i>	
1st Case	{ 1	2	826·6	173·4	7·0	75·9	83·2	7·3
	{ 2	3	836·0	164·0	6·1	64·4	87·3	6·2
2d    "	{ 1	2	799·2	200·8	6·7	108·4	78·9	6·8
	{ 2	3	806·2	193·8	7·3	101·9	78·2	6·4
3d    "	1	3	831·2	168·8	5·0	73·6	83·0	7·2
4th   "	{ 1	5	788·7	211·3	4·7	119·1	80·7	6·8
	{ 2	8	796·9	203·1	5·0	110·7	80·5	6·9
5th   "	1	3	762·9	230·4	3·6	139·4	80·2	7·2

The large amount of corpuscles associated with the slight increase of fibrin in the fifth case is explained by the circumstance of the attack being very mild, and the constitution particularly strong. The reverse is seen in the first case, in which the blood was taken from a woman who had been scrofulous from her youth.

The serum contains, on an average, 7·8% of inorganic constituents; just the same amount as in acute rheumatism.

[Blood, in a case of erysipelas of the hand, analysed by Rindskopf, yielded 7·71 of fibrin. The blood-corpuscles were not determined.

In a case of erysipelas in the face, occurring in a young man aged 20 years, recorded by Heller, the blood separated into 618·96 parts of clot and 351·04 of serum. The clot was tolerably firm, and covered with a buffy coat. The serum was of a fawn colour, and turbid, in consequence of suspended hæmatoglobulin. It contained no biliphæin.

The blood contained in 1000 parts :

Water . . . .	762·44
Solid constituents . . . .	237·56
Fibrin . . . .	5·45
Blood-corpuscles . . . .	141·71
Solid residue of serum . . . .	90·40]

### γ. *Phthisis tuberculosa*.

It is a well-known fact that the blood of phthical patients exhibits the ordinary characters of inflammatory blood.

The clot is usually rather small, consistent, and covered with a buffy coat: the serum is clear, and of a bright yellow colour. The blood differs considerably during the progressive stages of the disease.

Andral and Gavarret observe that, whatever be the stage of the disorder at which the blood is analysed, the fibrin seems always on the increase, and the corpuscles on the decrease; but the proportion of the increase on the one hand, and decrease on the other, varies with the progress of the disease. If the tubercles are still in a crude, unsoftened state, the increase of fibrin is only small, and its whole amount may be estimated at about 4; and the decrease in the amount of corpuscles, although perceptible, is by no means great. As the tubercles begin to soften, the quantity of fibrin usually increases to about 4·5, while the amount of corpuscles continues on the decrease. Subsequently, upon the formation of vomice in the lungs, the fibrin rises to 5·5, and sometimes even to 5·9: it never, however, attains the height observed in pneumonia. In the very last stage of the disease, as the blood becomes poor, the fibrin diminishes

in much the same ratio with the other solid constituents, and sometimes falls even under the healthy standard. Generally speaking, it seems that the amount of fibrin attains its maximum about the period when the febrile symptoms are regularly established.

I have made three analyses of the blood of phthysical persons, the results of which are not devoid of interest.

	Analysis 26.	Analysis 27.	Analysis 28.
Water . . . . .	807·500	825·200	750·000
Solid residue . . . .	192·500	174·800	250·000
Fibrin . . . . .	4·600	6·500	a trace
Fat . . . . .	2·350	4·200	3·750
Albumen . . . . .	98·360	90·350	131·000
Globulin . . . . .	71·230	61·110	94·500
Hæmatin . . . . .	3·110	2·690	2·750
Extractive matters and salts	9·350	8·000	15·250

The blood in analysis 26 was taken from a man aged 36 years, in the second stage of tubercular phthisis, who afterwards sunk under the disease. The blood in analysis 27 was taken from a man aged 41, in the third stage of the disease, who suffered extremely from nocturnal colliquative sweats, and from feverish symptoms. In these two instances the blood exhibits the characters of hyperinosis, for the quantity of fibrin is in one instance twice, and in the other thrice the normal amount, and the amount of hæmatoglobulin is below the healthy standard: moreover, the quantity of solid constituents is less than in healthy blood. Andral and Gavarret's observations respecting the changes that the blood undergoes as the disease advances are here borne out.

The 28th analysis gives results quite at variance with the two former. The blood in this instance was taken from a man about 30 years of age, who was treated in our hospital for tubercular phthisis. He had taken cod-liver oil for some time with much benefit; subsequently, however, frequent attacks of hæmoptysis came on, for which venesection was always immediately prescribed. The clot in these cases was seldom very firm. I analysed the blood taken at his last venesection. It was received into a shallow vessel, and amounted to between six and seven ounces. It did not coagulate, and it presented the appearance of a homogeneous dark red fluid, in which some white gelatinous flocks of coagulated fibrin were swimming.

The blood contained, much to my surprise, a larger amount of solid constituents than I have ever observed in any other analysis. The fat, when isolated, smelt strongly of the volatile fatty acid of the cod-liver oil, the odour of which was also strongly developed during the evaporation of the blood to dryness. A considerable quantity of hæmaphæin was present, and deeply coloured the extractive matters and salts. It is very probable that the peculiar changes in the blood in this instance are due principally to the cod-liver oil and to the repeated bleedings.

Andral and Gavarret have analysed the blood in 21 cases of this disease. Their maximum of fibrin was 5·9, their minimum 2·1. In only two instances did the amount of corpuscles approximate to the normal standard, as fixed by Lecanu: in these two cases it was represented by 122·1 and 120·4 respectively. The amount was frequently below 100, and the decrease of corpuscles was almost always found to be accompanied with a corresponding increase of fibrin.

The maxima, minima, and average of the various constituents, as deduced from 22 analyses, made by Andral and Gavarret, are given in the following table:

	Water.	Solid residue.	Fibrin.	Blood-corpuscles.	Solid residue of serum.
Maxima .	845·8	225·0	5·9	122·1	105·4
Minima .	775·0	154·2	2·1	76·7	65·1
Mean .	809·7	190·3	4·4	100·5	85·3
Healthy blood	890·0	210·0	3·0	127·0	80·0

This table shows the great difference that may exist between the quantities of the solid constituents, and of the corpuscles, in healthy and in diseased blood.

[Becquerel and Rodier examined the blood of nine persons affected with pulmonary phthisis, viz. five men and four women.

The following table represents the mean composition of the blood of the men:

	1st Venesection.	2d Venesection.	3d Venesection.
Density of defibrinated blood .	1056·7	1055·5	1050·3
Density of serum . . .	1028·0	1026·3	1025·5
Water . . . . .	794·8	799·8	821·0
Solid constituents . . .	205·2	200·2	179·0
Fibrin . . . . .	4·8	4·2	3·6
Fat . . . . .	1·554	1·443	1·060
Albumen . . . . .	66·2	65·0	62·0
Blood-corpuscles . . .	125·0	122·7	103·5
Extractive matters and salts .	7·7	6·7	8·9



Mean composition of the blood of phthisical women :

Density of defibrinated blood . . . . .	1055·4
Density of serum . . . . .	1028·2
Water . . . . .	796·8
Solid constituents . . . . .	203·2
Fibrin . . . . .	4·0
Fat . . . . .	1·729
Albumen . . . . .	70·5
Blood-corpuscles . . . . .	119·4
Extractive matters and salts . . . . .	7·6 ]

δ. *Febris puerperalis.*

[The blood in this disease has been analysed by Heller : it was of a very dark brown colour, but coagulated in the ordinary manner : the serum was turbid, but after standing for some time became clear ; its reaction was alkaline, its specific gravity 1025, and it contained no biliphæin. The clot was dark, of a loose consistence, and covered with a strong buffy coat, over which there was a delicate membrane, that presented under the microscope a finely granular appearance, and fat-vesicles.

In 1000 parts of blood there were contained :

Water . . . . .	833·85
Solid constituents . . . . .	166·15
Fibrin . . . . .	5·16
Blood-corpuscles . . . . .	77·52
Albumen and extractive matters . . . . .	77·47
Fixed salts . . . . .	6·00

The blood has been partially analysed in two cases of this disease by Becquerel and Rodier.

In the first case the blood, taken at the first venesection, yielded fibrin (4·3), albumen (55·6), and blood-corpuscles (77·3) : at the second venesection, the fibrin was (4·2,) the albumen (5·4), and the blood-corpuscles (66·6). The cholesterin and the phosphates exceeded the normal amount.

In the second case, the fibrin was normal, the albumen (43), and the blood-corpuscles (70).]

ε. *Eclampsia. Convulsions.*

[The blood of a girl, aged 20 years, who frequently had 40 or 50 attacks in the course of 24 hours, was subjected to several analyses by Heller.

The blood taken on the first occasion was of rather a dark colour, the clot was loose, and the serum was turbid and light red, in consequence of the presence of hæmatin. The specific gravity of the serum was 1030, and the relation of the clot to the serum as 446 : 554.

The blood contained in 1000 parts :

Water	. . . . .	797·00
Solid constituents	. . . . .	203·00
Fibrin	. . . . .	6·00
Blood-corpuscles	. . . . .	92·36
Albumen with extractive matters	. . . . .	96·03
Fixed salts	. . . . .	8·35

A second venesection was instituted 33 days afterwards. The physical characters of the serum were much as on the former occasion, except that its specific gravity was only 1025. The blood was taken partly from the arm, and partly from the foot.

The blood from the arm separated into 598·4 parts of clot, and 401·6 of serum, and was composed of :

Water	. . . . .	800·06
Solid residue	. . . . .	199·94
Fibrin	. . . . .	4·44
Blood-corpuscles	. . . . .	113·16
Residue of serum	. . . . .	82·35

The blood from the foot separated into 568·6 parts of clot, and 431·4 parts of serum, and was composed of :

Water	. . . . .	778·43
Solid constituents	. . . . .	221·57
Fibrin	. . . . .	5·84
Blood-corpuscles	. . . . .	125·80
Residue of serum	. . . . .	89·93

In the blood from the foot, the clot was covered with a buffy coat of about two lines in thickness ; in the blood from the arm there was no indication of that phenomenon.

Heller likewise analysed the blood in a case of convulsions occurring a few hours after delivery. At the period of the venesection there were symptoms of metropéritonitis and endometritis.

The blood was of a tolerably bright red colour, and separated on coagulation into 587·3 parts of clot, and 412·7 of serum. The specific gravity of the latter was 1026, and it contained a large quantity of biliphæin.

The blood contained in 1000 parts :

Water	.	.	.	.	.	788.20
Solid residue	.	.	.	.	.	211.80
Fibrin	.	.	.	.	.	5.87
Blood-corpuscles	.	.	.	.	.	124.07
Residue of serum	.	.	.	.	.	81.86]

ζ. *Carcinoma medullare colli uteri.*

[The sanguineous discharge from the uterus of a woman, aged 34 years, presenting all the characters of intense anæmia, was analysed by Drs. Lenzberg and Morthier. It was of a dark red colour, and the separation into clot and serum was not very perfect. There appeared, however, to be about 543 of the former, and 457 of the latter.

The blood consisted of :

Water	.	.	.	.	.	832.46
Solid constituents	.	.	.	.	.	167.53
Fibrin	.	.	.	.	.	16.44
Blood-corpuscles	.	.	.	.	.	77.03
Residue of serum	.	.	.	.	.	74.06

Here we see that there is an enormous increase of fibrin, and a great diminution of the corpuscles, while the residue of the serum remains almost normal.]

*On the probable cause of the peculiar change in the composition of the blood in inflammatory diseases.*

Although, in consequence of the deficiency of our knowledge regarding the true nature of inflammation, an attempt to explain the primary causes of the change undergone by the blood during this process may be deemed precipitate, yet the announcement of an opinion (though it have no higher claim than a mere hypothesis) may be of service in directing the attention of other investigators to the subject.

Numerous observations have shown us that blood retained for any length of time in an organ, and thus prevented from meeting with a due supply of oxygen, becomes poorer instead of richer in fibrin ; whereas there is undoubted evidence that in inflammation the fibrin is increased. Moreover, blood impeded in the course of the circulation becomes darker, (a sign that there is not a due supply of oxygen,) while blood in inflamma-

tion is generally brighter than in the normal state. The solid constituents of inflamed blood are certainly diminished, but the increased amount of fibrin renders it more plastic; so that we are not justified in comparing it (as Magendie has done) with blood in which the capacity of coagulating has been lessened by water, or alkaline carbonates, and which produced in the various organs, symptoms resembling those of inflammation. This defibrinated blood presents characters entirely the reverse of what we observe in inflammatory fluid, and resembles the condition of the circulating blood in typhoid fevers. We can, I think, scarcely doubt that the blood in an inflamed organ differs in its composition from the blood in the rest of the body, provided we can assume that there is a stagnation of blood in the affected organ during the whole period of inflammatory action.

Whether the blood is the first part of the system that becomes diseased, or whether it becomes modified in consequence of the pathological condition of the suffering organ, is a question not easily answered. This much, however, is certain, that whatever be the inflamed organ, the blood invariably differs from its normal condition in the same manner, although with varying intensity. If we direct our attention to the reaction of the whole organism during inflammation, we see that all the organs essential to the well-being of the blood are disturbed; the temperature of the whole body is heightened; the pulse is full, hard, tense, and frequent; the urine scanty and loaded. Under all these circumstances, we must expect to find a considerable deviation of the blood from its normal condition.

If, in this general reaction of the whole system, which corresponds with a heightened amount of vitality in the blood, a more rapid circulation is induced, we shall, without much difficulty, be enabled to give a sufficient explanation of the manner in which the peculiar changes already adverted to, are brought about.

The vital activity of the blood is heightened, and its metamorphosis hastened, by an increased rapidity of the circulation; it remains, then, for us to consider what effect an accelerated metamorphosis will have on the composition of the blood.

The metamorphosis of the plasma during the process of nutrition in the peripheral system will not necessarily be increased by an accelerated circulation; since (as I have endeavoured to show, in page 148,) the plasma remains virtually passive, and



is only changed by the cells of the organs, through which it passes, possessing the inherent power of abstracting and appropriating from it the substances requisite for their nourishment. It is different, however, with the active metamorphosis of the blood, in which the corpuscles are changed at the expense of the plasma. If the general circulation be hastened, the blood will be urged more frequently through the lungs and other organs that exert a modifying influence on its composition.

Hence the blood (passing more frequently through the lungs) gives off a larger amount of carbon in the form of carbonic acid than in the normal condition. If, as I have endeavoured to show (pp. 155 and 219), the blood-corpuscles take an essential part in the respiratory process, and their vital activity, evolution, and revolution are only carried on with the cooperative agency of the atmospheric origin, then, in proportion to this increased cooperation, will their development be hastened, their vitality heightened, and more corpuscles be consumed than in the normal state.

Two important conclusions may be drawn from my theory, regarding the production of fibrin from the blood-corpuscles, viz. that the amount of fibrin is increased, and of blood-corpuscles diminished. This is the more striking, since the increase of fibrin during the development of the corpuscles does not keep pace with its consumption in the act of peripheral nutrition, and since the supply of blood-corpuscles afforded by the chyle cannot be proportionate with the diminution produced by the accelerated circulation.<sup>1</sup>

Hence, if we only assume that the circulation is increased by the reaction of the organism in inflammatory affections, an explanation is at once afforded us of the change that occurs in the composition of the blood in hyperinosis, and at the same time of its heightened temperature. We do not, however, mean to imply that the increased circulation is the sole cause of the change in the blood, for it can hardly be denied that the nerves exert an influence on its constitution; moreover, as we have already shown, venesection modifies its characters.

<sup>1</sup> It has been suggested that blood in which there is an excess of fibrin increases the energy of the heart's action, while blood deficient in fibrin diminishes it. The rapid circulation of the blood in inflammations and its torpid condition in certain typhoid affections seems in favour of this view.

SECOND FORM OF DISEASED BLOOD: HYPINOSIS.<sup>1</sup>

I have shown, in speaking of hyperinosis sanguinis, what striking changes in the blood are due to the excessive accumulation of fibrin, and a corresponding diminution of blood-corpuscles. These differences are easily seen, because it is usually necessary that blood should be taken at a period when these changes are most obvious. In hypinosis sanguinis the case is different: in many diseases of this nature it is not customary to abstract blood at all, or at any rate only when an inflammatory affection is also present. Its distinctive characters are therefore seldom so decidedly marked as in the former case, and, in point of fact, less is known regarding this form of diseased blood.

*Chemical characters of the blood.*

The quantity of fibrin is frequently less than in healthy blood, or if it amounts to the normal quantity, its proportion to the blood-corpuscles is less than is found in a state of health (2·1 : 110 *Simon*, or 3 : 110 *Lecanu*); the quantity of corpuscles is either absolutely increased, or their proportion to the fibrin is larger than in healthy blood: the quantity of solid constituents is also frequently larger than in the normal fluid.

*Physical characters of the blood.*

The clot is most commonly large (but sometimes small), soft, diffuent, and of a dark, almost black red colour: occasionally no clot is formed. The buffy coat is seldom seen, and when it does occur it is thin and soft, or forms a gelatinous particoloured deposit on the clot. The serum is sometimes of a deep yellow tinge, from the colouring matter of the bile, or red, from blood-corpuscles in suspension: the blood has always an alkaline reaction.

From the numerous analyses of Andral and Gavarret, and from the observations of others, it appears that the blood occurs in a state of hypinosis in fever; if, however, the reaction assumes the synochal type, or if inflammation of the respiratory

<sup>1</sup> Formed from  $\psi\pi\sigma$  and  $\iota\gamma, \iota\nu\sigma\varsigma$ , the fibre of flesh.

or other organs supervene, then the fibrin will increase in a corresponding degree, and the blood-corpuscles decrease, so that the blood will approximate in its constitution to the normal standard, or even partially assume the characters of hyperinosis.

*a. Typhus abdominalis.*

The blood in this disease exhibits the characters of hypinosis perhaps more distinctly than in any other affection: but the statements regarding its qualitative and quantitative composition are still very contradictory, arising, probably, in part, from its varying in different stages of typhus: thus, in the period of excitement, it may incline towards a state of hyperinosis; in the stage of depression, the fibrin gradually decreases; and lastly, in the stage of collapse, the quantity of blood-corpuscles and of solid constituents decreases so remarkably, that in the case of putrid abdominal typhus the blood (in consequence of the liquor sanguinis being too watery, and deficient in salts) assumes the state of spanæmia. The same appears to occur in petechial typhus.

One source of difference is therefore evidently dependent upon the stage of the disease at which the blood is taken: the presence of any inflammatory symptoms will also modify its constitution.

The blood in typhus is found to be very deficient in fibrin, and frequently also in albumen: it coagulates imperfectly, and often remains in a semi-fluid state: the clot is soft, friable, of a very dark, almost black red colour, and is very rarely covered with a buffy coat: this form of blood becomes putrid sooner than the healthy fluid.

I have made two analyses of the blood in rather mild forms of the disease. The results do not by any means give a good idea of hypinosis sanguinis.

	Analysis 29.	Analysis 30.
Water . . . . .	816·875	792·340
Solid residue . . . . .	183·125	207·660
Fibrin . . . . .	2·525	2·010
Fat . . . . .	2·233	2·200
Albumen . . . . .	90·650	80·330
Globulin . . . . .	75·205	99·510
Hæmatin . . . . .	3·985	5·300
Extractive matters and salts . . . . .	9·678	12·670

The disease diagnosed in both instances (which occurred in our hospital) was dothinenteritis.

In both cases venesection was ordered at an early stage of the disease, when there was a good deal of vascular excitement present, which may account for the partial decrease of the fibrin and increase of the corpuscles.

The blood in analysis 29 was taken from a man 30 years of age; the tongue was furred, abdomen tender on pressure, mind tolerably clear; pulse rather full, 95 in the minute.

The blood in analysis 30 was taken from a man 38 years of age, in whom there was a good deal of nervous excitement, giddiness, and buzzing of the ears; the abdomen was tender on being pressed, the tongue thickly coated, and the pulse quick, rather hard and full. Both cases turned out favorably.<sup>1</sup>

The most comprehensive researches on the blood in typhoid fever (*fièvres typhoïdes*<sup>2</sup>) are those of Andral and Gavarret, who made 50 analyses of blood taken from 20 persons suffering under this affection.

The following are their principal results:

The fibrin never rises perceptibly above the normal standard in true typhoid fever. It often remains at the normal height, and is still more frequently below it.

In inflammatory disorders it is pretty clear that the fibrin increases with the increased intensity of the disease: here we observe just the reverse: the fibrin decreases in proportion to the advancement of the disorder.

Andral and Gavarret observe that this cannot be ascribed to the repeated bleedings, or to the continued low diet, for these circumstances induce no change in the amount of fibrin in other diseases. As soon, however, as any symptoms of convalescence appear, the fibrin begins to increase, even before the organization could contribute a supply by increased nutriment. This continues to be the case during the progress of convalescence, and as the patient improves the corpuscles simultaneously decrease.

In inflammatory diseases we observed a general tendency to

<sup>1</sup> [In an analysis of the blood in typhus abdominalis, made subsequently to the publication of his Chemistry, Simon found, water 887·5, solid constituents 112·5, fibrin none, albumen 54, hæmatoglobulin 47·25.]

<sup>2</sup> *Fièvre continue qui reconnaît pour caractère anatomique l'inflammation exanthématique, puis ulcéreuse, des follicules intestinaux.* (Andral.)



diminution in the corpuscles : here we have just the reverse, for the more frequently we analyse blood soon after the outbreak of the disease, the more frequently shall we find instances in which the corpuscles, instead of being diminished, are considerably increased, and, even in the more advanced stages, the amount of the corpuscles is frequently found to exceed, or at any rate to equal, the normal quantity.

The absolute increase of the corpuscles is not, however, so decided as the increase of the fibrin in inflammatory diseases ; neither is it so essential a condition for the existence of the disease, for even in those cases in which the amount is much increased at the commencement of the disorder, it may become diminished during its course, and even when it is getting more severe. However, when the absolute quantity of the corpuscles is diminished, its proportion to the fibrin is still greater than is ever observed in the normal state.

The leading characteristic of the blood in this disease is the decrease of the fibrin, which diminishes in proportion to the violence of the attack, and from which another character is derived, namely, the increased amount of corpuscles. During the early period the diminution of the fibrin is not absolute ; it is only relative in relation to the corpuscles ; but as the disease approaches its height, the diminution becomes absolute.

Researches instituted in mild cases may give perfectly negative results.

Their maximum of fibrin was 3·7 ; their minimum ·9. It is true that in one case they found 4·2 of fibrin, but the blood was taken during convalescence.

The maxima, minima, and average results of 41 analyses are given in the following table :

	Water.	Solid residue.	Fibrin.	Blood-corpuscles.	Solid residue of serum.
Maximum .	862·3	243·7	4·2	149·6	98·0
Minimum .	756·3	137·7	0·9	66·7	66·8
Average .	796·0	204·0	2·6	116·0	77·9
Healthy blood .	790·0	210·0	3·0	127·0	80·0

This average of 41 analyses (I have omitted some, as giving no definitively clear result) does not give the general characters of the blood, as it is expressed in the majority of the analyses. The amount of fibrin is certainly less than in healthy blood, but the corpuscles do not attain their normal height. If, however,

the fibrin is estimated at 3·0, the proportion of the corpuscles is 134, which is higher than in healthy blood.

The quantity of the residue of the serum, and of solid constituents generally, approximates closely to the normal standard.

The inorganic constituents of the residue of the serum amount, on an average, to 7·6%, which is very little lower than the corresponding number in erysipelas or rheumatism.

Reid Clanny states, however, that the quantity of salts is materially diminished in typhoid blood.

The following table contains the numerical results of Andral and Gavarret's researches on the blood in typhoid fever. In order to make the proportion of the corpuscles to the fibrin more striking, I have given not merely the numbers obtained from the analyses, but the relative numbers on the assumption that the fibrin is constantly represented by 3.

Venesection.	Date of attack.	Water.	Solid constituents.	Fibrin.	Blood- corpuscles.	Blood- corpuscles. (Fibrin = 3.)	Residue of serum.	
1st Case	1	5	756·3	243·7	2·3	145·3	180·0	96·1
	2	7	769·7	230·3	2·1	135·8	193·0	92·4
	3	8	785·2	214·8	1·8	126·2	210·0	86·8
	4	10	798·6	201·4	1·3	116·2	268·0	83·9
	5	15	827·4	272·6	1·0	91·7	273·0	79·9
2d	1	?	819·7	180·3	0·9	93·1	310·0	86·3
3d	1	5	752·9	247·1	2·4	146·7	183·0	98·0
4th	1	7	766·5	233·5	2·5	143·6	172·0	87·4
	2	9	777·6	222·4	3·7	136·2	110·0	82·5
	3	12	782·1	217·9	3·6	134·5	112·0	79·8
5th	1	8	767·6	232·4	5·0	139·3	83·0	88·1
	2	10	777·3	222·7	5·4	129·7	72·0	87·6
	3	11	782·4	217·6	5·0	127·1	76·0	85·5
	4	14	791·7	208·3	4·0	123·6	92·0	80·7
6th	1	9	769·5	230·5	3·6	149·6	124·0	77·3
	2	10	784·7	215·3	2·9	125·3	129·0	87·1
	3	12	804·3	195·7	2·3	123·7	161·0	69·7
	4	15	831·1	168·9	1·9	103·0	163·0	64·0
	5	33	845·5	154·5	3·7	79·6	64·0	71·2
7th	1	9	810·3	189·7	3·4	102·4	90·0	83·9
	2	10	816·2	183·8	3·5	105·0	90·0	79·8
	3	12	825·6	174·4	2·3	93·9	122·0	78·2
	4	17	836·8	163·2	1·7	86·3	152·0	75·2
	5	24	847·8	152·2	2·1	76·0	108·0	74·6

From these two columns of the blood-corpuscles we see that the decrease of the fibrin is almost always connected with the

increase of the corpuscles, so that the proportion between the two gradually differs more and more from the normal mixture.

The exceptions to this rule are caused either by some inflammatory complication, as in the fifth case, where an acute attack of bronchitis accompanied the fever, or by the patient being in a state of convalescence as in the fifth analysis, in cases 6 and 7.

Andral and Gavarret offer no explanation of the peculiarities in the fourth case.

The solid constituents of the blood are more frequently above than below the normal standard, but the proportion is a fluctuating one, and dependent, as we shall presently see, on the progress of the disease.

Lecanu has analysed the blood of two persons suffering from typhoid fever. As he did not determine the amount of fibrin, the proportion of that constituent to the corpuscles cannot be shown. Their absolute quantity is less than in normal blood. Lecanu also states, that he thinks that a paucity of corpuscles may be inferred from the smallness and friability of the clot,<sup>1</sup> a statement at variance with the researches of Andral and Gavarret.

Lecanu also found a diminution of the solid constituents generally:—

<sup>1</sup> I may take this opportunity of saying a few words regarding the possibility of drawing a correct inference respecting the amount of fibrin and of corpuscles from the clot. We are justified in assuming the existence of a great quantity of fibrin from a large and very firm clot, and a small amount from a small diffuent clot. We cannot, however, with the same accuracy, draw similar inferences respecting the amount of corpuscles. On receiving the blood of a cachectic horse into a high cylindrical glass and into a shallow vessel, a large and very firm clot generally forms in the latter (unless, as is sometimes the case, the blood-corpuscles sink during coagulation), and little serum is expressed; while, in the other vessel, two distinct layers are observed, a large one, consisting of firmly coagulated fibrin, containing serum, below which there is a much smaller layer, consisting of semifluid blood-corpuscles. As the albumen inclosed in the coagulated fibrin in the high glass forms a very solid mass resembling a pseudopolypus or buffy coat, we see that, independently of the corpuscles, a very firm clot may be formed; indeed, in inflammatory blood, this is often observed to a greater or lesser degree. There may, consequently, be as many blood-corpuscles in a small and loose clot as in a large and firm one; moreover, we usually find numerous corpuscles suspended in the serum and deposited at the bottom of the vessel, in addition to those contained in the clot, in blood deficient in fibrin. The relative amount of corpuscles and of fibrin in clots of different size and consistence is a subject worthy of investigation.

Water . . . . .	805.20	795.88
Solid residue . . . . .	194.80	204.20
Blood-corpuscles . . . . .	115.00	105.00
Residue of serum . . . . .	79.00	99.12

Chomel does not consider that the diminution of fibrin is a specific character of the blood in typhoid fever, because he found that in 6 out of 30 cases, the blood formed a solid clot, covered with a buffy coat, but differing in thickness and colour from the inflammatory clot; while in 2 cases there was a slight film, beneath which the clot was diffuent, in 2 the blood remained perfectly fluid and slightly lumpy, and in 20 the blood formed a firm clot, but no buffy coat.

The blood in all these cases was taken during the first or the commencement of the second stage, never in the third. The peculiarities in Chomel's statement may be partly due to the blood being taken at a period before the fever had reached its height, partly to the association of some inflammatory symptom, or to a more synochal type of the disease.

According to Jennings,<sup>1</sup> the blood in the first stage of typhoid fever (depression) is generally thick and dark; it coagulates rapidly and forms a soft, large, dark-coloured clot. In the second stage (excitement) it flows readily, is of a scarlet colour, does not coagulate so quickly as, and forms a more solid clot than the former. It is also occasionally covered with a slight buffy coat. In the third stage (collapse) it flows very readily, is thin, watery, and of a dark colour: the clot is loose and flocculent, and occasionally appears more as a sediment of colouring matter than as a clot. In thoroughly developed typhus, Dr. Armstrong found the blood of the temporal artery as dark as that of the vein. Dr. Clanny also states that the watery portion of the blood increases with the intensity of the disease, and that not merely the solid constituents generally, but also the salts and carbonic acid are diminished. The water begins to decrease, and the solid constituents to increase in favorable cases after 12 or 18 days. According to Stevens, the salts of the blood (especially the chloride of sodium) are diminished in all typhoid fevers.

<sup>1</sup> Course of Lectures on the Physiology and Pathology of the Blood, by H. Ancell. The Lancet, 1840, p. 338.



[Becquerel and Rodier have analysed the blood of 13 persons attacked with typhoid fever, 11 men and 2 women. Of the 11 men, 6 were bled once, 4 twice, and 1 thrice; of the 2 women, 1 was bled once, and 1 thrice.

The following table exhibits the mean composition of the blood of the male patients, obtained at the first venesection:

Density of defibrinated blood . . . . .	1054.4
Density of serum . . . . .	1025.4
Water . . . . .	797.0
Solid residue . . . . .	203.0
Fibrin . . . . .	2.8
Fat . . . . .	1.773
Albumen . . . . .	64.8
Blood-corpuscles . . . . .	127.4
Extractive matters and salts . . . . .	6.3

The salts consisted of:

Chloride of sodium . . . . .	2.9
Other soluble salts . . . . .	2.5
Phosphates . . . . .	0.497
Iron . . . . .	0.555

The fibrin varied considerably, the maximum being 4.9, while in three cases it was considerably below the normal standard. The albumen and blood-corpuscles were, in most instances, diminished.

Four of the same men were bled a second time, and the following table gives the mean results of the blood obtained in these four cases, on both occasions:

	1st Venesection.	2d Venesection.
Density of defibrinated blood . . . . .	1054.0	1051.4
Density of serum . . . . .	1025.0	1024.7
Water . . . . .	801.0	814.5
Solid constituents . . . . .	199.0	185.5
Fibrin . . . . .	2.3	1.3
Fat . . . . .	1.527	1.408
Albumen . . . . .	64.4	62.0
Blood-corpuscles . . . . .	124.5	113.5
Extractive matters and salts . . . . .	6.0	7.3

The salts consisted of

Chloride of sodium . . . . .	3.6	3.5
Other soluble salts . . . . .	2.6	2.7
Phosphates . . . . .	0.544	0.255
Iron . . . . .	0.581	0.519

A comparison of the two columns shows that the blood ob-

tained by the second venesection contains a considerably smaller mean amount of fibrin than the blood previously taken. The albumen and corpuscles are likewise diminished.

The case in which venesection was performed three times offered no peculiarity; neither did the analyses of the blood of the two women.

In all these analyses the clot was found to present no striking peculiarity. There was none of the softness and diffulence on which the older writers laid so much stress.

Scherer has analysed the salts of the blood in a case of typhoid fever. In 1000 parts of blood there were 176·3 of solid residue, which on incineration yielded 11·92 of fixed salts. These consisted of:

Chloride of sodium	.	.	.	.	6·82
Carbonate of soda	.	.	.	.	1·41
Sulphate of soda	.	.	.	.	0·84
Phosphate of soda	.	.	.	.	0·94
Carbonate of lime	.	.	.	.	0·16
Phosphate of lime	.	.	.	.	0·60
Sulphate of lime	.	.	.	.	0·22
Peroxide of iron	.	.	.	.	0·60]

### β. *Febris continua*.

1. *Prodromi febris continuæ*. The blood exhibits similar changes in the progress of continued fever, as in typhus. Andral and Gavarret have carefully analysed the blood in this disease, and give the following account of their researches.

They made nine analyses of the blood of six persons. The fibrin did not exceed the normal amount in any instance, (in one, however, it amounted to 3·2); in three cases it was a little below the standard, but exceeded 2; in two cases it was rather less than 2; and in one case as low as 1·6. The amount of blood-corpuscles was lower in only two cases than in normal blood; in the others it was more or less increased, and in the blood in which the fibrin amounted to only 1·6, the corpuscles amounted to 157·7, which, if the fibrin were estimated at 3, would give the enormous amount of 296. We have only one instance in typhoid blood of so high a proportion. The amount of the residue of the serum is increased, rather than diminished, and the same is the case with the solid constituents of the blood generally.

Their analyses gave the following results :

Venesection.	Date of the disease.	Water.	Solid residue.	Fibrin.	Blood- corpuscles.	Residue of serum.	
1st Case	1	7	766.2	233.8	3.0	143.5	87.3
2d „	1	8	769.5	230.5	1.8	136.4	92.3
3d „	1	8	761.3	238.7	2.9	142.7	93.1
4th „	1	15	770.8	229.2	3.2	137.9	88.1
5th Case	{	1	785.6	213.4	2.3	125.4	86.7
		2	788.3	211.7	2.2	124.0	85.5
		3	790.8	209.2	2.1	123.0	84.1
6th Case	{	1	744.2	255.8	1.6	157.7	96.5
		2	779.7	220.3	2.1	129.3	88.9

The inorganic constituents of the residue of the serum amounted on an average to 7.5%, which corresponds with the proportion in typhoid fever.

2. *Febris continua.* Andral and Gavarret made 21 analyses of the blood of 11 persons suffering from continued fever. They divide their analyses into two series, one containing the results obtained when the blood was taken nearly at the termination of the disease; the other, when certain inflammatory states, as for instance angina, bronchitis, erysipelas, &c. had supervened.

These researches exhibit less of the characters of hypinosis than those instituted on the blood at the commencement of continued fever, which, in the first series may be due to the circumstance of the disease being on the decline; and in the second, to the inflammatory complication.

In both series the fibrin exceeds the normal amount, and in both, the amount of corpuscles is, in part, also below the standard.

The following analyses are taken from the first of these tables :

Venesection.	Date of disease.	Water.	Fibrin.	Blood- corpuscles.	Residue of serum.	
1st Case {	1	4	725.6	3.3	185.1	86.0
	2		789.3	3.3	128.3	79.1
2d „ {	1	8	824.9	3.2	82.5	89.4
	2	11	833.7	3.1	77.2	86.0
	3	17	851.9	4.2	62.4	81.5

The blood in the first of these cases was taken from a man aged 58 years. The amount of the corpuscles, especially when the age of the patient is considered, is very surprising; it is

the highest amount ever found by Andral and Gavarret. In the second case, the patient was at the same time suffering from chlorosis, which accounts for the small number of corpuscles.

The second table does not give very clear results, on account of the inflammatory complications.

Venesection.	Date of disease.	Water.	Fibrin.	Blood- corpuscles.	Residue of serum.	
1st Case {	1	9	793·8	4·3	114·7	87·2
	2	12	801·9	3·6	109·8	85·0
	3	19	810·0	5·0	95·9	89·1
2d „	1	15	758·9	3·8	160·7	76·6
3d „	1	20	784·2	2·6	131·0	83·2
4th „	1		804·8	5·4	94·1	95·7
5th „ {	1		791·4	3·1	118·6	86·9
	2		810·1	4·0	101·8	83·1
	3		824·3	3·7	86·9	85·1

In the first of these cases the fever was complicated with a rather severe attack of angina. In the third analysis in this case, the blood contained a large quantity of fibrin due to a renewal of the inflammatory symptoms in a rather violent form. Slight erysipelas of the face was present in the second case; in the third there was swelling and redness of the tonsils; in the fourth the fever was complicated with acute bronchitis; in the fifth the blood was taken from a woman three months after delivery: at the period of the second venesection, some slight symptoms of meningitis had appeared.

Jennings<sup>1</sup> has analysed the blood of a girl aged 14 years, suffering from continued fever. He found it composed of:

Water	. . . .	856·0
Solid residue	. . . .	144·0
Fibrin	. . . .	2·0
Fat	. . . .	3·0
Albumen	. . . .	37·0
Blood-corpuscles	. . . .	91·0
Extractive matter	. . . .	3·0
Alkaline salts	. . . .	3·8
Earthy salts	. . . .	1·0

[Becquerel and Rodier have analysed the blood of 3 men and 2 women suffering from ordinary continued fever. The mean

<sup>1</sup> Course of Lectures on the Physiology and Pathology of the Blood, by H. Ancell. The Lancet, 1840, p. 339.



composition of the blood of the 3 men is given in the following table:

Density of defibrinated blood	.	.	.	1056.8
Density of serum	.	.	.	1025.5
Water	.	.	.	781.6
Solid constituents	.	.	.	218.4
Fibrin	.	.	.	2.8
Fat	.	.	.	1.7
Albumen	.	.	.	65.7
Blood-corpuscles	.	.	.	142.4
Extractive matters and salts	.	.	.	5.8

Here we see that the fibrin and albumen remain nearly normal, while the corpuscles, instead of diminishing, are slightly above the average (their numbers being 146, 142, and 138.) The fatty matters and salts offered no peculiarity.

They give the following particulars regarding the blood of the two female patients.

The corpuscles were augmented (135.5) in the first case; normal (125.5) in the second: fibrin normal (1.9) in the first; doubled (3.6) in the second: albumen normal (73 and 70) in both. The serum was turbid in both cases. In the case in which the corpuscles were 125, the clot was firm and resisting, in the other it was soft and diffuent.]

In the following exanthemata, which, with true erysipelas, constitute Schönlein's family of *Erysipelacea*, we find that the composition of the blood is very similar to what it is in continued fever; the characters of hypinosis are much less marked than in the typhoid form. Some analyses give negative results, while in others the tendency of the constitution of the blood is more towards hyperinosis than hypinosis.

The maximum of fibrin amounts to only 4.4, against which there is a minimum of 1.1. In the majority of cases it does not differ much from Lecanu's normal average 3.

The blood-corpuscles are increased in a less degree in variola and varioloid, than in scarlatina and rubeola.

#### *Variola et morb. varioloid.*

The blood was analysed by Andral and Gavarret in 5 cases of true variola and 2 of varioloid disease.

In all the cases of variola the eruption was confluent. The

blood-corpuscles differed but little from their normal standard, but the quantity of fibrin varied considerably, although the increase above the normal mean was only small. It is worthy of remark that the quantity of fibrin appears to increase, although only slightly, by repeated bleeding; a circumstance which, according to Andral and Gavarret, characterizes the phlogoses.

This may be due to the inflammatory state of the skin in this disease, although we do not perceive a similar occurrence in typhoid fever, in which the mucous surface of the intestine is in a somewhat similar state.

Their analyses gave the following results :

	Venesection.	Water.	Fibrin.	Blood-corpuscles.	Residue of serum.
1st Case	{ 1	771.5	4.4	120.6	103.5
	{ 2	780.8	2.9	110.2	106.1
	{ 3	820.2	3.2	94.6	82.0
2d "	{ 1	791.3	3.0	114.3	91.4
	{ 2	803.9	3.2	92.6	100.3
	{ 3	811.8	3.0	88.4	96.8
	{ 4	817.3	3.3	87.0	92.4
3d "	{ 1	781.4	2.6	127.9	88.1
	{ 2	792.0	3.5	124.4	80.1
4th "	{ 1	796.0	4.1	126.5	76.4
	{ 2	792.7	2.0	124.9	80.4
5th "	1	805.0	2.9	98.8	92.3

The residue of the serum contained on an average  $7.0\frac{0}{0}$  of inorganic constituents.

In the first case, the first bleeding was ordered at the commencement of the disease, during the febrile period; the second at the commencement, and the third at about the middle of the eruptive stage. In the second case, the first bleeding was ordered some days before the appearance of the disease; the second during the fever; the third on the third day of the eruption, and the fourth on the sixteenth day of the eruption. In the third case, the first bleeding was ordered at the commencement of the eruption; the second during the suppurative stage. In the fourth case, both venesections were prescribed during the height of the eruption. In the fifth case the pustules were filled with blood (*variole hémorragique*;) the bleeding was ordered when the eruption was at its height.

The analyses of blood in varioloid gave the following results :

Water.	Fibrin.	Blood-corpuscles.	Residue of serum.
785.6	2.3	120.3	91.8
782.1	2.4	125.8	89.7

The residue of the serum contained 7·6% of inorganic matter in the second analysis.

In the first instance the bleeding was performed on the 3d day; and in the second case on the 2d day of the eruption.

*Rubeola. (Morbilli.)*

Andral and Gavarret found that in the measles the fibrin never exceeded, nor did it ever fall much below Lecanu's average. In most cases the corpuscles were above the normal standard. I quote the following analyses from their researches :

	Venesection.	Day of eruption.	Water.	Fibrin.	Blood-corpuscles.	Residue of serum.
1st Case	1	3	760·2	2·6	146·6	90·6
2d	„ 1	2	766·9	3·0	140·9	89·2
3d	„ 1	3	781·6	2·6	137·1	78·7
4th	„ { 1	2	786·7	2·5	137·5	73·4
	„ { 2	-	795·8	2·7	131·6	70·1
5th	„ { 1	2	792·1	2·4	118·6	86·9
	„ { 2	-	823·2	3·4	93·3	80·1

The residue of the serum contained on an average 8·4% of inorganic constituents, which was one of the highest amounts that occurred in the course of their researches.

The patient in case 3 had also been bled on the first day of the eruption: the second bleeding in case 4 was performed on the second day after the disappearance of the eruption.

The young woman from whom the blood in case 5 was taken, presented so strongly the general appearances of anæmia in consequence of excessive menstruation, that the amount of corpuscles, 118·6, may be regarded as very high: the second venesection was performed after the disappearance of the eruption, and when symptoms of tubercular phthisis were very apparent.

*Scarlatina.*

Andral and Gavarret have made four analyses of the blood of three persons suffering from scarlatina. Two of these analyses decidedly indicate the character of hypinosis, although not in a very marked degree. The two other cases present differences which will be presently explained :

	Venesection.	Water.	Fibrin.	Blood-corpuscles.	Residue of serum.
1st Case	{ 1	761·5	3·1	146·0	89·4
	„ { 2	782·6	4·0	124·3	89·1
2d	„ 1	776·3	3·5	136·1	84·1
3d	„ 1	798·3	6·8	112·2	82·7

The first bleeding in the first case was ordered on the second day of the eruption; the second during convalescence. At this period a number of boils had appeared, and there was considerable fever, to which two circumstances the change in the blood is attributable.

The bleeding in the second case was ordered on the second day of the eruption.

Lecanu<sup>1</sup> has also made two analyses of the blood in this disease, and has obtained nearly similar results.

	Blood of a man aged 35 years.	Blood of a man aged 18 years.
Water . . . .	776.55	770.41
Blood-corpuscles . . . .	144.55	146.80
Residue of serum . . . .	78.90	82.79

The quantity of fibrin was not determined by Lecanu.

### *Febris intermittens.*

From the analyses made by Andral and Gavarret of the blood in this disease, we are led to conclude that instead of being in a state of hypinosis, the blood exhibits rather a tendency towards hyperinosis. Andral and Gavarret themselves remark, that in consequence of the absence of all disturbance in the normal functions of the organism during the remission of the febrile symptoms, it might be concluded *a priori* that no peculiar changes would be exhibited in the blood.

The fibrin rises a little above the normal average; the corpuscles, however, with the exception of one case in which the bleeding was ordered at the commencement of a second attack, fall below the normal proportion. The blood in most of these cases was, however, taken from persons suffering from long standing tertian or quotidian fever.

The period at which the blood was taken, whether during the remission, the hot or the cold stage, seemed to exert no influence on the composition of the fluid.

It will be sufficient to give the maxima, minima, and mean of their researches.

<sup>1</sup> Etudes chimiques, etc., p. 97.



	Water.	Solid residue.	Fibrin.	Blood-corpuscles.	Residue of serum.
Maximum .	847.9	221.9	3.8	127.9	91.0
Minimum .	778.1	152.1	3.0	68.8	71.6
Mean of 7 analyses	811.4	188.6	3.3	104.3	80.0

The loss of a considerable quantity of blood by hemorrhage must necessarily influence the composition of the blood remaining in the system. This will be shown (as we have already seen in the Phlogoses) by the diminution of the corpuscles, and in most cases of the fibrin also.

From the blood taken from the body we can usually draw a pretty safe inference regarding the composition of the blood remaining in the system: a thick, readily coagulating blood usually indicates an abundance of the circulating fluid, and especially a considerable quantity of corpuscles and fibrin, while a thin non-coagulating blood implies a deficiency of those two constituents.

The blood does not, however, exhibit the same changes of composition in all the diseases that are classed as hemorrhages. On the contrary, it has been shown by Andral and Gavarret that the composition of the blood in spontaneous cerebral hemorrhage is similar to that which is so characteristic in typhoid fever.

#### *Hæmorrhagia cereбрalis.*

Andral and Gavarret found that the quantity of fibrin in the majority of cases of apoplexia cereбрalis, and of the cerebral congestion known as the forerunner of that disease, was less than in healthy blood; the amount of corpuscles was, however, frequently absolutely increased, and, excepting in a few cases, was larger, in proportion to the fibrin, than in the healthy fluid. The solid constituents were generally rather increased; circumstances which all correspond with a state of hypnosis.

These points are most strikingly seen in certain cases of of spontaneous cerebral hemorrhage, when, for instance, in correspondence with the small amount 1.9 of fibrin no less than 175.5 of corpuscles were found.

Andral and Gavarret have made eight analyses of the blood of 7 persons suffering from this affection. Their results are given in the following table:—

Venesection.		Period from commencement of disease.	Water.	Solid residue.	Fibrin.	Blood-corpuscles.	Residue of serum.
1st Case	1	1	790.9	209.1	2.2	135.9	71.0
2d	" {	3	742.3	257.7	1.9	175.5	80.3
		6	779.2	220.8	3.5	137.7	79.6
3d	" 1	3	770.8	229.2	2.6	140.6	86.0
4th	" 1	4	791.8	208.2	3.9	126.5	77.8
5th	" 1	8	806.9	193.1	2.0	120.8	70.3
6th	" 1	—	791.3	208.7	2.1	122.4	84.2
7th	" 1	5	774.0	226.0	3.2	123.4	99.4

The residue of the serum contained, on an average, 7.9% of inorganic constituents, which shows that the quantity of salts is not diminished.

The blood in the first case was taken from a woman aged 60 years, whose feet had been œdematous for six months, in consequence of hypertrophy of the heart.

The second case was that of a woman aged 59 years, who, two days before the bleeding, had a severe apoplectic fit: the blood exhibited decided symptoms of hypnosis, the fibrin being diminished, and the corpuscles and (to a very considerable degree) the solid constituents being increased. The bleeding was repeated three days afterwards, when consciousness had returned, and at this period the corpuscles were found to have diminished in a very striking degree, being about 25% less than on the former occasion: the fibrin in the meantime increased in a still more rapid proportion.

Andral and Gavarret observe, in regard to this case, that the slight cerebral hemorrhage is not sufficient to account satisfactorily for the change in the composition of the blood that was observed on the second occasion; moreover, since the loss of blood is not always necessarily followed by a diminution of fibrin, it may be asked whether the changed composition of the blood, instead of being a consequence, may not have been a cause of the disease, since blood deficient in its proper quantity of fibrin has always a tendency to escape from the vessels.<sup>1</sup>

The change in the composition of the blood is proportional

<sup>1</sup> In opposition to this view it may be stated that blood containing uninjured corpuscles cannot be effused unless there are orifices in the parietes of the vessels, and it is questionable whether blood abounding in fibrin can escape through such pores at all, while blood deficient in that constituent can pass through with facility. The only constituent that can permeate the walls of uninjured vessels is hæmatoglobulin dissolved in liquor sanguinis; and this solution is not produced by a diminution in

to the violence of the attack, as is seen in the third case, where the fibrin is only slightly diminished, although the corpuscles are considerably increased.

Consciousness remained in the fourth and fifth cases. The increase of the fibrin, while the corpuscles remained stationary, is deserving of notice in the former of these cases. In the sixth case the hemorrhage had occurred three weeks before the venesection, and was followed by entire hemiplegia of the left side. In the seventh case the patient had previously been bled on the third day of the attack ; she had retained her consciousness.

Andral and Gavarret have made 21 analyses of the blood of 15 persons suffering from cerebral congestion (the usual prodromus of spontaneous cerebral hemorrhage). Its symptoms are intense headache, giddiness, and a tendency towards epistaxis.

In the majority of these cases the fibrin was found to be below the normal quantity. It twice rose to 3·7, once to 3·5, and once to 3·2 ; in all the other cases it was below the normal amount, and it occurred as low as 1·6.

The amount of blood-corpuscles was pretty near the standard average ; in two instances it rose to 152 and 154 ; and in two other cases, (the one a woman of weakly condition, and the other a person under the noxious influence of lead,) it fell to 88.

I shall only give the maxima, minima, and mean of these researches :

	Water.	Solid constituents.	Fibrin.	Blood-corpuscles.	Residue of serum.
Maximum .	820·3	259·8	3·7	152·3	104·8
Minimum .	740·2	179·7	1·6	88·3	76·4
Mean . .	787·1	212·9	2·6	120·0	89·7
Healthy blood	790·0	210·0	3·0	127·0	80·0

The residue of the serum contained, on an average, 7·9% of inorganic constituents, the same amount as in cerebral hemorrhage.

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No causes can be assigned with any degree of certainty to the peculiar modification of the blood to which I have assigned the term *hypinosis*.

the amount of fibrin, since the corpuscles are insoluble in defibrinated serum, provided a sufficient amount of chloride of sodium be contained in it. On the other hand, the solubility of the hæmatoglobulin in the liquor sanguinis and its consequent property of escaping through the walls of the vessels may arise from an absolute decrease of salts or from an increased amount of water in the blood. In the analyses quoted in the text the salts were not diminished.

The composition of the blood in hypinosis is essentially the reverse of that in hyperinosis. The amount of corpuscles is increased, that of fibrin diminished, and the solid constituents generally are increased rather than diminished; while in the phlogoses they are most commonly below the normal standard. We have seen in the previous analyses that in proportion as the febrile symptoms assumed the form of crethismus, the characters of hypinosis became less marked; and, on the other hand, that when they took on a torpid type these characters were more strikingly developed.

If we assume that the circulation of the blood is accelerated in inflammatory fever, we may regard it as impeded in torpid fever. In the one case, the blood abounding in fibrin acts as an increased stimulus to the heart; in the other, the heart partially loses its power of action. Its contractions succeed each other, it is true, with increased rapidity, but the blood-wave, propelled at each systole, is diminished and powerless, and the pulse, although much quickened, is small and wiry.

In consequence of the delay thus occasioned in the motion of the general mass of the blood, oxygen cannot act so efficiently on it as in the normal state of the circulation, and consequently the blood does not possess the bright red colour observed in inflammatory affections, but is dark, and the temperature, instead of being increased, is often diminished, as has been observed by Schönlein, in typhus. Hence the metamorphosis of the blood, instead of being accelerated, as in hyperinosis, is impeded, and consequently the ratio of the corpuscles to the albumen is reversed. In abdominal typhus, the amount of the corpuscles is rendered more striking, by the diminution of albumen, which constituent is removed from the blood by the profuse diarrhœa that accompanies this disease.

From these observations it is very probable that the primary cause of this modification of the blood may, in a great measure, be referred to the impeded circulation, and to the deficient energy of the heart's action, which may be regarded as indications of the depressed vitality of the blood itself; but at the same time the influence of the nerves on its composition and on the circulation (although how they act we know not) must not be overlooked.

Finally, it must be observed that the state of hypinosis is



not a permanent one ; it lasts only for a brief period, till the blood either begins to exhibit more vital activity, and to return towards its normal condition ; or, if its vitality be still more depressed, till it assumes the character of spanæmia. The preponderance of the corpuscles is not absolute (as in plethora<sup>1</sup>), but merely relative, and is due, partly to their hindered consumption, and partly (as is seen in abdominal typhus) to an absolute diminution of the water and the albumen. If the fever assume a malignant torpid character, the hypinosis speedily merges into spanæmia.

### THIRD FORM OF DISEASED BLOOD : SPANÆMIA.<sup>2</sup>

The chemical and physical relations of the blood in those states in which it is deficient in solid constituents, and especially in fibrin and blood-corpuscles, are not yet accurately known.

We have less frequent opportunities of examining this condition of the blood, for some of the diseases in which it occurs are of rare occurrence, and in the other more common forms, the prudent physician avoids as much as possible increasing by venesection the general want of blood in the system.

#### *Chemical characters of the blood.*

The amount of fibrin and of corpuscles is diminished : the amount of residue of serum is either normal or diminished : the proportion of water is higher than in healthy blood : the amount of salts in the serum is sometimes normal, sometimes diminished.

#### *Physical characters of the blood.*

The blood is very fluid ; it is sometimes of a dark or even violet, and sometimes of a bright colour ; it usually coagulates imperfectly, sometimes not at all. The clot is small, soft, diffuent, and neither covered with a true nor false buffy coat. The serum is generally of a bright yellow colour, but sometimes of a dark yellow or even red tint. The specific gravity of the blood is considerably diminished.

<sup>1</sup> [Becquerel and Rodier have recently shown that this opinion is erroneous, and that, in plethora, the amount of the blood is increased, while its composition is unaffected.]

<sup>2</sup> From αίμα, blood, and σπανός, or σπάνιος, poor ; spanæmia, poverty of the blood. We prefer this term to anæmia, because the latter is used to represent a morbid condition of the blood subordinate to spanæmia.

This form of diseased blood appears capable of being subdivided into two classes: one embracing diseases primarily dependent upon the chylipoietic viscera, such as are due to bad food, deficient and improper formation of chyle, atmospheric influences, protracted action of poisonous mineral agents (lead, mercury and its compounds, chlorine, iodine, &c.) ; and finally, to inordinate consumption of the blood through a deficiency of the animal fluids.

The corpuscles, which, as we have seen, are of the utmost importance in the blood, are either not produced in sufficient quantity, or are consumed in a quicker proportion than they are reproduced. The liquor sanguinis, although poor in fibrin, may yet contain a sufficient quantity of albumen and salts to prevent the relatively increased quantity of water from dissolving the corpuscles.

All the diseases arranged by Schönlein under the family *cyanoses* belong to this subdivision.

The other subdivision embraces certain diseases characterized by the peculiar composition of the blood, but in which the primary causes of its change of composition are quite distinct from those which act in the *cyanoses*, and are probably dependent upon the central nervous system. A peculiar state of the atmosphere (most likely due to certain changes in its chemical composition), protracted wars, the effluvia of decaying animal matter, &c., are assigned as the external causes of the production of these disorders, the principal of which are abdominal typhus, petechial typhus, the yellow fever, and the plague.

In the cyanoses, as also in the malignant (putrid) form of typhus, passive hemorrhages are by no means rare.

It has been asserted that the deficiency of fibrin and of corpuscles renders the blood liable to exude through the walls of the vessels. It is clear, however, that the colouring matter cannot escape through the walls of the capillaries, unless such a change occurs as to render the hæmatoglobulin soluble in the liquor sanguinis, since perfect corpuscles are not capable of passing through the uninjured walls of the vascular system. As the blood which is discharged by epistaxis in the *morbus maculosus Werlhofii* (as well as menstrual blood) contains corpuscles, the walls of the vessels must be imperfectly closed. Such a form of blood appears to occur in the putrid form of abdominal or petechial typhus. The hæmatoglobulin becomes soluble in the liquor sanguinis, in consequence of a deficiency in the due proportion

of salts, and an excess of water ; in this case we may therefore speak of a red, bloody transudation.

#### I. CYANOSSES.

##### *Anæmia and hydræmia.*

The blood in anæmia is essentially different from the normal composition. If the anæmia has arisen from excessive loss of blood, we may fairly assume that the total mass of that fluid has diminished. This, in fact, constitutes true anæmia. The composition is, however, also changed ; it is poor in corpuscles and in fibrin, because these constituents are not so easily supplied as the albumen, which may be obtained at once from the lymphatics. The quantity of the solid constituents is also found to be diminished, if the quantity of the corpuscles is (either absolutely or relatively) decreased: the quantity of water is therefore increased, which induces the state of the blood known as hydræmia. Anæmia and hydræmia cannot be well separated, as a decrease in the solid constituents is usually produced by every loss of blood.

If the anæmia is caused by abnormal or deficient chylification, the proper quantity of liquor sanguinis may be present, while the corpuscles and fibrin are diminished: in this case, also, the absolute quantity of solid constituents is lessened.

The decrease of the solid constituents will probably attain its maximum under the combined influences of an unhealthy humid atmosphere, and improper, unsuitable nourishment. Under these circumstances the blood will resemble a viscid, light-coloured watery fluid.

I have not analysed the blood in any cases of anæmia, but it is usually described as clear, watery, and viscid. The clot, if it forms at all, is small, soft, and diffuent ; the fibrin, after it has been separated by whipping, is not tough and firm, but soft and viscid, and in the same state as it occurs in the chyle. The serum is slightly coloured and transparent. It has not been accurately ascertained whether the salts are decreased or in a normal proportion.

In hydræmia, the serum (as has been observed by Ansell<sup>1</sup>), is usually transparent, and contains only a small quantity of

<sup>1</sup> Course of Lectures on the Blood. The Lancet, 1840, p. 667.

colouring matter, and probably only a slight amount of salts.<sup>1</sup> Geddings<sup>2</sup> observes regarding the inhabitants of the morasses of the Carolinas, in whom anæmia, or, more correctly speaking, hydræmia, is developed in a high degree, that the temperature of the body is reduced, that the respiration is short and laborious, and that the pulse is small, tremulous, and frequent. In the examination of the heart and larger vessels of anæmic persons he found either scarcely any coagulated blood, or else a clear red, or greenish dirty-looking fluid, almost entirely devoid of solid or colouring constituents, containing but few blood-corpuscles, and which could not be coagulated either by heat or by nitric acid. This watery fluid was frequently present in considerable quantity.

#### *Carcinoma.*

In a case of cancer of the left lobe of the liver, and of the pylorus, accompanied with atrophy of the spleen, occurring in a man, aged 53 years, the blood contained :

Analysis 31.	
Water . . . . .	887.2
Solid constituents . . . .	112.8
Fibrin . . . . .	3.0
Albumen . . . . .	55.1
Blood-corpuscles . . . .	45.8
Extractive matters and salts .	8.9

#### *Scrophulosis.*

In scrofulous affections the blood is deficient in solid constituents, especially in fibrin and in corpuscles. The primary causes are probably due to a deficient formation of chyle, and to the influence of a moist unhealthy atmosphere.

Dubois<sup>3</sup> has analysed the blood of scrofulous persons. The blood coagulates slowly, the clot is small, soft, and diffuent ; the serum is thin, and often of a red colour. When examined under the microscope, some of the corpuscles appeared devoid of colour at the edges only, some entirely colourless. Their size was not materially changed, but they appeared flattened, spherical, or cylindrical. Hence we may also infer that there is a deficiency in the quantity of salts in the blood of scrofulous persons.

<sup>1</sup> The blood-corpuscles would, however, be dissolved in this case.

<sup>2</sup> Baltimore, Med. and Surg. Journal, 1834, No. 4.

<sup>3</sup> L'Expérience, 1839, No. 87.



*Chlorosis.*

The blood in this disease possesses the general characters of this fluid in anæmia. The clot is small, sometimes soft, but frequently of the normal consistence: the serum is bright, slightly coloured, and tolerably clear. The fibrin (separated by whipping) is not so dense and consistent as in normal or in inflammatory blood. Its quantity is normal, or only slightly diminished, while the amount of the corpuscles is considerably decreased, and the solid constituents generally are less than in healthy blood.

Golding Bird<sup>1</sup> states, however, that the blood in chlorosis forms just as solid a clot as in inflammatory diseases, and Jennings<sup>2</sup> observed even a buffy coat on the clot of chlorotic persons in the absence of all inflammatory symptoms. He accounts for this phenomenon by supposing that as, in chlorosis, the amount of fibrin is normal, but that of the corpuscles much diminished, the ratio of the fibrin to the corpuscles may be the same as in inflammatory disorders.

Andral and Gavarret state that the blood in chlorotic persons forms a clot similar to the coagulum in healthy blood, and that a buffy coat is not unfrequently observed on it.

I found, on the contrary, that the clot in chlorosis was very soft, and that the fibrin was not so firm as in inflammatory diseases. These contradictions are easily explained by supposing that the chemico-physical characters of the blood change during the progressive development of the disease. We can obtain a more accurate knowledge of the stage of development of the disease from the blood than from many other diagnostic signs.

I am indebted to Dr. Vetter for the following specimen of the blood of a chlorotic girl, which gave, on analysis, the following results:

	Analysis 32.	Healthy blood.
Water . . . .	871·500	795·278
Solid constituents . .	128·500	204·022
Fibrin . . . .	2·080	2·104
Fat . . . .	2·530	2·346
Albumen . . . .	79·820	76·660
Globulin . . . .	30·860	103·022
Hæmatin . . . .	1·431	6·209
Extractive matters and salts	11·000	12·012

The hæmatoglobulin contained  $4\frac{4}{10}$  of colouring matter.

<sup>1</sup> Ansell, Course of Lectures, &c. The Lancet, 1840, p. 887.

<sup>2</sup> Ibid.

The girl was 19 years of age, moving in a respectable station, and tall; she exhibited all the symptoms of unmixed, long-standing chlorosis, which appeared in this instance to have reached its highest development.

On contrasting it with healthy blood, we find little difference in the absolute quantity of fibrin; this constituent is, however, extremely large when considered relatively with the corpuscles, or with the solid constituents generally.

The quantities of albumen and of extractive matters and salts do not differ very much from the quantities in healthy blood.

Andral and Gavarret have analysed the blood in several cases of this disease. It is different in the incipient and in the fully-developed stages of chlorosis.

In the former the appearance of the patient hardly indicates the presence of the disease; the face is blooming, rather than pale, and the blood merely exhibits a very considerable decrease of the corpuscles.

The following numbers give the maxima, minima, and mean of 8 analyses, made during this stage.

	Water.	Solid constituents.	Fibrin.	Blood-corpuscles.	Solid residue of serum.
Maximum .	816.3	210.0	5.3	112.7	94.1
Minimum .	790.0	183.7	2.4	97.7	76.5
Mean . .	801.0	199.0	3.5	106.8	88.0
Healthy blood, according to Lecanu }	790.0	210.0	3.0	127.0	80.0

When the disease is fully developed the fibrin is slightly diminished, but the quantities of blood-corpuscles, and of the solid residue generally are very much lessened.

Andral and Gavarret have made 12 analyses of the blood of 9 cases of confirmed chlorosis.

I shall give the maxima, minima, and mean results of these analyses; omitting, however, the cases that were complicated with inflammatory symptoms.

	Water.	Solid residue.	Fibrin.	Blood-corpuscles.	Residue of serum.
Maximum .	868.7	181.3	3.6	95.7	100.9
Minimum .	818.5	131.5	2.1	38.7	75.4
Mean . .	853.2	146.8	2.9	56.7	88.0

The blood in which the corpuscles attained their minimum, had the following composition :

Water . . . . .	868.7
Solid constituents . . . .	131.3
Fibrin . . . . .	3.5
Blood-corpuscles . . . . .	38.7
Solid residue of serum . . .	89.1

The amount of corpuscles exceeds, in only three cases, the number 60 : and in five cases it remains below 50 : the fibrin remains in five cases below 3, and in the other five cases it amounts to or exceeds 3, the maximum being 3.6. The amount of the solid residue of the serum is in almost every case rather above the normal standard. It follows from 4 analyses, in two of which, however, the chlorosis was combined with tubercular phthisis and rheumatism, that the residue of the serum contains on an average 8.2 of inorganic constituents. The two cases of pure chlorosis gave the inorganic constituents of the residue of the serum at 8.9, while the two complicated cases gave only 7.6, so that it appears as if the salts were rather increased than diminished in this disease. Others, however, assert that there is a diminution of the salts.

[The following table gives the mean composition of the blood of six chlorotic girls, as determined by Beequerel and Rodier :

Density of defibrinated blood . . . . .	1045.8
Density of serum . . . . .	1028.1
Water . . . . .	828.2
Solid constituents . . . . .	171.8
Fibrin . . . . .	3.4
Fat . . . . .	1.5
Albumen . . . . .	72.1
Blood-corpuscles . . . . .	86.0
Extractive matters and salts . . . .	8.8

The salts consisted of :

Chloride of sodium . . . . .	3.1
Other soluble salts . . . . .	2.3
Phosphates . . . . .	0.441
Iron . . . . .	0.319]

My own observations, as well as those of Andral and Gavarret, on the blood of chlorotic persons who had been taking ferruginous medicines, are especially interesting.

The girl from whom the blood of analysis 32 was taken, took 2 ounces of the tincture of iron and 64 grains of metallic iron, during a period of seven weeks, commencing with the day of the first venesection.

The blood which was then analysed had the following constitution :

Analysis 33.	
Water . . . .	806.500
Solid residue . . . .	193.500
Fibrin . . . .	1.200
Fat . . . .	2.299
Albumen . . . .	81.230
Globulin . . . .	90.810
Hæmatin . . . .	4.598
Extractive matters and salts	9.580

The hæmatoglobulin contained 4.8% of colouring matter.

This change in the composition of the blood is truly surprising, and affords an excellent illustration of the wonderful effects of certain remedies. The amount of solid constituents is increased by nearly one half, and the increase of the hæmatoglobulin is likewise extraordinary. In this, as well as in Andral and Gavarret's observations, the quantity of the fibrin is diminished: the proportion of the hæmatin to the globulin is however slightly, although not materially, increased.

The changes in the condition of the patient kept pace with those of the blood. Before, she was pale, and her lips colourless; now she presented a really blooming appearance. Andral and Gavarret have arrived at perfectly analogous results.

They give two cases, in one of which the iron was administered for four weeks, in the other for only three weeks.

*1st Case.*

	Previous to use of the iron.	After use of the iron.
Water . . . .	866.5	818.5
Fibrin . . . .	3.0	2.5
Blood-corpuscles . . .	46.4	95.7
Residue of serum . .	83.9	83.3

*2d Case.*

Water . . . .	852.8	831.5
Fibrin . . . .	3.5	3.3
Blood-corpuscles . . .	49.7	64.3
Residue of serum . .	94.0	100.9

[The two following analyses were made by Herberger.<sup>1</sup> The blood in (1) was taken from a chlorotic girl aged 20 years; in

<sup>1</sup> Buchner's Repertorium, 2d series, vol. 29.



(2) it was taken from the same girl after an eight weeks' course of chalybeates.

In both instances the blood formed a tolerably large clot, but no buffy coat.

	1.	2.
Water . . . .	868·340	807·080
Solid constituents . .	131·660	192·920
Fibrin . . . .	3·609	1·950
Fat . . . .	2·310	2·470
Albumen . . . .	78·200	81·509
Globulin . . . .	36·470	94·290
Hæmatin . . . .	1·590	4·029
Extractive matters and salts .	8·921	8·236]

Andral and Gavarret have likewise analysed the blood of a chlorotic man. They made three analyses of it at intervals of four weeks each. During this time he had been taking iron, but without any marked advantage :

Venesection.	Water.	Fibrin.	Blood-corpuscles.	Residue of serum.
1	810·1	3·6	87·9	98·4
2	831·5	3·4	77·2	87·9
3	819·4	3·7	86·9	90·0

The blood of chlorotic persons has also been analysed by Lecanu<sup>1</sup> and Jennings.<sup>2</sup> The following are the results of their analyses.

	<i>Lecanu.</i>		<i>Jennings.</i>	
	1.	2.	1.	2.
Water . . . .	862·40	861·97	871·0	852·0
Fibrin . . . .			5·0	3·0
Blood-corpuscles .	55·15	51·29	48·7	52·0
Residue of serum .	82·45	86·74		
Albumen . . . .			60·0	78·0
Fat . . . .			1·7	2·0
Extractive matters			3·0	2·0
Alkaline salts .			7·6	7·0
Earthy salts .			1·8	2·0

Andral and Gavarret consider that the great rarity of cases of hemorrhage in chlorotic persons is due to the amount of fibrin remaining normal, while the blood-corpuscles are considerably diminished. I cannot, however, think that the primary cause of ordinary hemorrhage is only to be sought for in the peculiarities of the blood. That a lesion of the vessels occurs in

<sup>1</sup> Etudes chimiques, etc., p. 113.

<sup>2</sup> The Lancet, 1839-40, p. 887.

the majority of cases of hemorrhage is obvious from the circumstance of blood-corpuscles being found in the effused fluid. I cannot easily conceive how blood, deficient in fibrin, should more readily escape from the vessels than blood abounding in that constituent.

In passive hemorrhages, the relations of the tissues themselves ought to be taken into account as much as the quality of the blood.

[Becquerel and Rodier analysed the blood of two girls, in whom all the symptoms of chlorosis existed, (including the *bruit de diable* in the carotids,) and yet there was no diminution of the corpuscles, or of the solid constituents generally.

	1st Case.	2d Case.
Density of defibrinated blood . . . . .	1055·4	1055·4
Density of serum . . . . .	1027·9	1027·2
Water . . . . .	798·6	792·7
Solid constituents . . . . .	201·4	207·3
Fibrin . . . . .	2·9	2·3
Fat . . . . .	1·287	1·980
Albumen . . . . .	66·8	70·5
Blood-corpuscles . . . . .	123·8	126·4
Extractive matters and salts . . . . .	6·6	5·8

The salts consisted of,

Chloride of sodium . . . . .	2·6	3·9
Other soluble salts . . . . .	2·2	3·4
Phosphates . . . . .	0·329	0·427
Iron . . . . .	0·492	0·516]

### *Scorbutus.*

[The blood has been analysed by Mr. Busk in three well-marked cases of scurvy that occurred in the Dreadnought Hospital Ship. Its composition is represented in the following table:

	1.	2.	3.	4. Healthy blood. (Busk.)
Water . . . . .	849·9	835·9	846·2	788·8
Solid constituents . . . . .	150·1	164·1	153·8	211·2
Fibrin . . . . .	6·5	4·5	5·9	3·3
Albumen . . . . .	84·0	76·6	74·2	67·2
Blood-corpuscles . . . . .	47·8	72·3	60·7	133·7
Salts . . . . .	9·5	11·5	10·9	6·8

These analyses are sufficient to disprove the general notion that in this disease the corpuscles are dissolved in the serum. In the blood taken from these scorbutic patients, the separation into serum and clot was as perfect and took place as rapidly as in healthy blood. In two of the cases the clot was buffed and cupped.]

*Morbus maculosus Werlhofii.*

[Porphyra hæmorrhagica (Mason Good.) Land-scurvy.]

I have analysed the sanguineous fluid discharged from the mouth of a girl aged 20 years. She was pale and weak, the pulse rather excited, breath fetid, and there were red spots on the gums and above the uvula, from which blood had apparently escaped. This sanguineous fluid contained much saliva, and some flocculi of mucus, but no fibrin. It had a faint, disagreeable smell, was of a very dark (almost black) red colour, transparent, and deposited an almost clear sediment. The decanted fluid exhibited no blood-corpuscles under the microscope, and only a few membranous granules. The sediment was composed of blood-corpuscles, which, for the most part, were changed from the flattened into a spherical form, and of which a small quantity were of a pale yellow colour, while the majority were almost, if not quite, colourless. Moreover, I observed a considerable quantity of epithelium-scales and mucus-granules, the latter of which were especially visible in the flocculi deposited at the bottom. After thoroughly stirring the fluid, it was boiled; upon which it coagulated perfectly. I found that it was composed of—

	Analysis 34.
Water . . . . .	948·889
Solid residue . . . . .	51·111
Fat . . . . .	1·377
Albumen and mucus . . . . .	34·032
Globulin . . . . .	5·610
Hæmatin . . . . .	0·102
Alcohol-extract, bilin, and salts . . . . .	4·635
Water-extract, ptyalin, and salts . . . . .	2·555
Biliverdin . . . . .	0·366

The presence of the bile in this blood, although I was as-

sured, both by the patient and the nurse, that there had been no vomiting when the blood was discharged, appeared to me of importance, since it is well known that a very small quantity of bile is sufficient to dissolve a considerable quantity of blood-corpuscles.

[Some observations on the sanguineous contents of the stomach, and on the blood found in the heart after death from this disease, occur in Heller's Archiv, vol. i, p. 10.]

### *Hemorrhages.*

I have already observed that continuous and excessive loss of blood must necessarily produce a change in the composition of that portion which remains in the system, and that there will be a more or less marked degree of spanæmia in proportion to the quantity of blood that has been lost.

Some researches have already been made regarding the chemico-physical condition of the blood which is separated from various organs in the different forms of hemorrhage.

I analysed the blood of a woman who was suffering from melæna. It was a thick fluid, of a dark red colour (nearly black), and gave off only a slight faecal odour: dilute acid heightened the colour, and caustic potash developed an odour of ammonia: it had a strong alkaline reaction, coagulated only imperfectly on heating, and threw out an unpleasant smell, not however resembling the odour of faeces. It did not coagulate upon standing, and contained no fibrin. No blood-corpuscles could be observed under the microscope, but merely some yellow particles floating in a clear fluid. It was very rich in fat and in hæmaphæin. The fat resembled in odour the fat of putrid blood. The alcohol-extract, which contained a considerable quantity of fat, had a very bitter taste, but when treated with sulphuric acid no bilifellinic acid was separated; consequently the presence of bile was undecided. Upon heating the dried residue a considerable quantity of ammonia was given off.



The blood contained in 1000 parts :

	Analysis 35.
Water . . . . .	886.200
Solid residue . . . . .	113.800
Brown fat . . . . .	9.000
Albumen . . . . .	39.830
Globulin . . . . .	36.530
Hæmatin . . . . .	3.018
Hæmaphæin . . . . .	2.220
Hæmaphæin with alcohol-extract, and salts .	9.673
Water-extract and salts . . . . .	10.355

The hæmaphæin left upon incineration a trace of peroxide of iron, and some carbonate of soda; the alcohol-extract left chloride of sodium and carbonate of soda; and the water-extract left chloride of sodium, carbonate of soda, sulphate of soda, and phosphate of lime.

The blood discharged in hæmatemesis is, according to Schönlein's observations, either clear and very fluid, or black and coagulated; sometimes the two forms are mixed. The taste of the blood is bitter if any bile is mixed with it, acid if the spleen is affected.

Ancell<sup>1</sup> states that vomited blood is often coagulated, of a dark brown or blackish colour (in consequence of the acids of the stomach); in other cases it resembles coffee-grounds.

In a girl, who brought up enormous quantities of blood, I found that it occurred, for the most part, in rather large brownish red coagula: the fluid had a faintly acid reaction, but on touching a section of a clot with red litmus paper, a blue tint was produced. The microscope revealed the presence of corpuscles in a state of good preservation.

In hæmaturia the blood is mixed with urine. If the quantity of the blood is very small, all the blood-corpuscles may become dissolved, as I have frequently observed. The urine, however, coagulates on heating, and the colour disappears after boiling, while discoloured flocculi are thrown down. The corpuscles are frequently preserved entire, and form a sediment, on allowing the urine to stand for some time. In this case they can be detected by the microscope.

<sup>1</sup> The Lancet, Sept. 1840, p. 842.

Lecanu<sup>1</sup> quotes an opinion of Delarive, that a change occurs in the colouring matter of the blood that escapes in hæmaturia, since sulphuric acid produces a brown-red instead of a black-red, and nitric and muriatic acids produce a white instead of a black-red precipitate: alcohol also produces a white deposit. These peculiarities in colour (especially the white precipitate) may probably be explained by the precipitation of the albumen, while in consequence of the dilution of the blood the hæmatoglobulin escapes precipitation.

*Purpura hæmorrhagica.*

[The blood has been analysed in a case of this disease by Routier<sup>2</sup>. In 1000 parts he found:

Water . . . .	795·244
Solid constituents . . . .	204·756
Fibrin . . . .	0·905
Blood-corpuscles . . . .	121·701
Residue of serum . . . .	83·405

From this analysis it appears that the blood does not assume the form of spanæmia. It is placed here in consequence of the analogy between purpura hæmorrhagica and the preceding diseases.]

*Typhus petechialis putridus. Yellow fever. Plague.*

The blood in these diseases is described as watery, very poor in fibrin, and of a dark colour. If any clot be formed, it is diffuent, and very soft: the serum is frequently of a deep yellow or brown-red colour, partly from the colouring matter of the bile, and partly from dissolved hæmatoglobulin. It possesses a very peculiar smell, which probably differs in each disease. It is by no means improbable that this smell may be produced by a volatile salt of ammonia.

Schönlein has directed attention to the formation of a peculiar gas that escapes with the blood in the post-mortem examination, on opening the large vascular trunks, and which is probably developed in the blood during the last stage of the disease.

Chomel also speaks of the development of a gas in the interior of the veins.

<sup>1</sup> Etudes chimiques, etc., p. 95.

<sup>2</sup> Gazette des Hôpitaux, vol. 6, No. 90.

Ancell<sup>1</sup> remarks, that in the first stage of the endemic yellow fever of the West Indies the blood is of a brighter red, contains more salts, and is hotter than in a state of health. As the disease progresses, its characters become changed, and towards the termination of the malady it loses its saline and animal principles, and becomes black and thin ; in which state sanguineous effusions occur from the different outlets and tissues.

Balard and Rochet<sup>2</sup> have made some observations on the properties of the blood in the plague.

Balard is of opinion that the lymphatic system is first disordered, and that inflammation, degeneration, and suppuration of the lymphatic ganglia and vessels follow. It is not until suppuration in these structures has fairly set in that the venous system begins to suffer, and a change in the composition of the blood to ensue.

The blood, when the disease is fully established, exhibits invariably the same properties, whether it is obtained by bleeding, or taken from the vessels after death. The arterial and venous blood have both the same dark colour ; the blood generally appears in a peculiar state of solution, and oily drops are frequently seen on its surface. It frequently has a peculiar smell, but never the buffy coat.

In three patients, aged 19, 23, and 27 years respectively, and in whom the blood was drawn between the third and fifth days, it was of a dark-brown colour, and in the course of two hours a good clot was formed. This, however, is frequently not the case, especially when the oily globules appear. The serum was reddish, and developed a gas which soon browned sugar of lead test-paper, and which therefore contained sulphuretted hydrogen. The clot constituted about 40%, and contained 33·5 of water, ·6 of fibrin, 3·8 of cruor, ·25 osmazome, ·9 of chlorides of sodium and potassium, and ·2 of carbonate of soda and fat.

Lachèze,<sup>3</sup> who observed the plague in Egypt, states that the blood never coagulates, that it is greasy, and of a black colour.

<sup>1</sup> Course of Lectures on the Physiology and Pathology of the Blood. The Lancet, 1840, p. 837.

<sup>2</sup> Casper's Wochenschrift, 1838, No. 12.

<sup>3</sup> Magendie, Leçons sur le Sang. Bruxelles, 1839, p. 200.

THE FOURTH FORM OF DISEASED BLOOD: HETEROCHYMEUSIS.<sup>1</sup>

I arrange under this form all those states of the blood in which a substance is present that does not exist in the normal fluid: when, for instance, the blood contains urea (in appreciable quantity), sugar, colouring matter of the bile, fat, or pus. The circumstances that lead to the establishment of this diseased condition of the blood are far less natural than those which are connected with the production of the three former classes. The arrangement is artificial, and merely adopted for convenience, since this class of diseases has simply this property in common, that the composition of the blood is here *qualitatively* changed, whilst in the three former it was only altered *quantitatively*. The putrid form of typhus, the yellow fever, and the plague, certainly might have been placed in this class, since colouring matter of the bile, and a salt of ammonia, are often found in the serum. I have, however, thought it best to place these diseases in the third class, because, in the first place, the presence of the abnormal constituents is not constant; and because, secondly, in consequence of the deficiency in the solid constituents of the blood in these disorders, they naturally occur under the class *spanæmia*.

## I. BLOOD CONTAINING UREA: URÆMIA.

a. *Morbus Brightii*.

Andral and Gavarret describe the blood in this disease as characterized by a deficiency of albumen in the serum.

It is evident, however, both from my own and from Christison's researches, that the decrease of the solid constituents of the serum is not always the leading character in this disease. I have thought it right, therefore, to arrange this disease, on account of the nearly constant presence of urea in the blood, under the form *heterochymeusis*.

Christison,<sup>2</sup> who has attentively studied the blood in this disease, describes it in the following manner: The blood in the first stage of the disease coagulates with a thick, firm, and cupped buffy coat. The serum is usually rather turbid, and when shaken

<sup>1</sup> From *ἕρερος* and *χύμενσις*.

<sup>2</sup> On the Granular Degeneration of the Kidneys, etc., by R. Christison. Edin. 1839.



with ether yields a small quantity of solid fat. The decrease in the density of the serum at this stage is very remarkable. While in healthy blood it is estimated at 1029—1031, it now sinks to 1020, or even 1019; and in connexion with this circumstance we find a large quantity of albumen in the urine.

Another very remarkable peculiarity is the presence of a certain quantity of urea in the serum.

The following changes occur in the progress of the disease: (1.) There is an excess of serum, the clot often constituting not more than one fourth of the blood. (2.) The density of the serum returns to its normal state, or even exceeds it; sometimes, however, it remains low, even in the advanced stages. (3.) The urea disappears as the disease advances, but usually reappears, towards the termination of the case, in even a larger amount than previously. (4.) The fibrin, which is increased in the first stage, returns to its normal amount as the disease advances, and only becomes considerable again during inflammatory complication. (5.) The most remarkable character of the blood in the advanced stage is the great decrease of blood-corpuscles, which frequently amount to only one third of the normal proportion.

I have analysed the blood in four cases of Bright's disease, and obtained the following results:

	Analysis 36.	Analysis 37.	Analysis 38.	Analysis 39.
Water . . . .	830.590	826.891	823.461	839.700
Solid constituents . .	169.420	173.109	176.539	160.300
Fibrin . . . .	7.046	3.060	5.000	3.500
Fat . . . .	2.403	1.860	2.520	2.680
Albumen . . . .	103.694	109.432	97.010	63.400
Globulin . . . .	40.151	41.300	54.090	71.300
Hæmatin . . . .	3.808	4.377	5.100	4.910
Extractive matters and salts	12.348	13.280	12.819	11.380

The blood in analysis 36 was taken from a man aged 40, who had been treated for some time in our hospital for this disease: traces of urea were detected in the extractive matters, by the method given in page 183.—The blood in analysis 37 was taken from a man aged 20, whose feet and arms were so œdematous as to render venesection a matter of some difficulty. Considerable quantities of urea were found in the blood.—The blood in analysis 38 was taken from a man aged 30, in whom the disease was not so advanced as in the former cases. A consider-

able quantity of urea was found in the serum, which exhibited a remarkable milk-white turbidity, not caused by fat in a state of suspension, but (as shown by the microscope) produced by numerous minute solid granules, which, by diluting the serum, and then allowing it to rest, were collected, washed, and analysed. They were not soluble in alcohol or in ether, but dissolved after a continuous digestion in dilute acetic acid, from which they were precipitated by ferrocyanide of potassium. Hence I concluded that they were fibrin.

The blood in analysis 39 was taken from a man 36 years of age, at the commencement of the disease. Hæmaturia had occurred a few days previous to the venesection. The quantity of urea in this blood was very considerable.—The urine was albuminous in all these cases, especially in the last two.

It is worthy of remark that I have found the hæmatoglobulin more abundant in hæmatin in these than in ordinary cases. It varied from 8 $\frac{0}{10}$  to 9·5 $\frac{0}{10}$ .

Christison gives the following results of analyses of blood in Bright's disease :

	Water.	Solid constituents.	Fibrin.	Blood-corpuscles.	Residue of serum.
1	863·8	136·2	2·8	57·4	76·0
2	844·1	155·9	4·4	57·7	93·8
3	808·3	191·7	3·0	133·9	54·8
4	831·0	169·0	2·8	111·1	55·1
5	836·3	163·7	2·7	104·6	56·4
6	825·2	174·8	4·3	95·5	75·0
7	859·2	140·8	8·2	75·5	57·2
8	885·3	114·7	6·2	56·4	52·1
9	862·8	137·2	3·2	72·1	61·9
10	855·5	144·5	4·5	42·7	97·3
11	862·6	137·4	8·5	72·8	56·1
12	887·0	113·0	5·6	49·1	58·3
13	841·6	158·4	3·4	91·6	63·4

Christison's average composition of healthy blood being :

775·7	224·3	3·8	137·1	83·4
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The blood in the 3d analysis was taken from a robust man, aged 55 years, in the first stage of granular degeneration, and suffering from anasarca. The urine was very albuminous, but not bloody : the serum was milky, and abounded in urea.

The blood in the 5th analysis was taken from a man aged 48, suffering from anasarca and continued fever. The kidneys were in the first stage of granular degeneration; the urine contained

a considerable quantity of albumen.—In the 6th case, the disease had reached the middle stage: the patient was at the same time suffering from anasarca and chronic catarrh: the blood contained urea.—In the 7th case, the disease was in the first stage; the patient (a man aged 42) was also suffering from peripneumonia and anasarca: the blood contained urea, and the urine was albuminous.

8th analysis. Blood of a youth aged 16 years, suffering from dropsy; kidneys in the middle stage of granular degeneration. The serum was peculiarly rich in solid constituents, and contained a considerable quantity of urea.

9th analysis. Blood of a man aged 23. The granular degeneration was more advanced, the blood contained urea.

10th analysis. Blood of a man aged 23, after having recovered from scarlatina. The disease in the kidneys was in an advanced stage: the blood was remarkable for the small quantity of corpuscles.

11th analysis. Blood of a woman aged 25 years, suffering from anasarca, catarrh, and chronic rheumatism. The degeneration of the kidneys was in a very advanced stage. The blood contained urea, and the urine was albuminous.

12th analysis. Blood of a man aged 32, suffering from pleuritis and anasarca; kidneys in an advanced stage of the disease. Blood remarkable for the small quantity of corpuscles, and for the large amount of urea.

13th analysis. Blood of a woman aged 56, with anasarca and ascites; the disease of the kidneys was in a very advanced stage.

These observations entirely coincide with my own, as far as regards the decreased quantity of solid constituents, the small amount of blood-corpuscles, as the disease advances, and the presence of urea in the blood.

Andral and Gavarret have analysed the blood of three persons with Bright's disease.

The following are their results:

	Venesection.	Water.	Solid constituents.	Fibrin.	Blood-corpuscles.	Residue of serum.
1st Case	1	801·0	199·0	1·6	127·6	69·1
2d    "	1	867·0	133·0	2·3	61·6	68·4
3d    "	{ 1	849·0	151·0	3·2	82·4	64·8
	{ 2	836·0	164·0	3·0	88·2	72·7
	{ 3	845·9	154·1	4·2	71·0	78·9

The second venesection in the 3d case was ordered at a time when the urine was less albuminous than it had been: the third was prescribed after a considerable interval, and when the urine contained no albumen.

### *β. Cholera.*

The researches of trust-worthy observers have shown that the blood in cholera exhibits the following peculiarities. The quantity of water is decreased, and consequently there is an increase in the amount of solid constituents arising, in all probability, from the watery alvine evacuations; the amount of fibrin, as well as the alkaline reaction, is diminished, and urea is found in the serum. The search after this substance has not always been successful, but its presence has been clearly shown by Rainy,<sup>1</sup> O'Shaughnessy,<sup>2</sup> Marchand,<sup>3</sup> and myself.

The following are the leading physical characters of the blood in this disease. It appears to be thicker than usual, and either forms a soft, friable clot, or else coagulates very imperfectly.

Wittstock has made a careful analysis of the blood during cholera. In its external characters it resembled healthy blood: the clot was of a scarlet red colour on the surface, but darker than usual in the interior.

His analysis gave the following results: serum 36·5%, clot 63·5%. The specific gravity of the serum was 1·0385, and 100 parts left 13·75 of solid residue. The clot, when treated with absolute alcohol, left a residue of 31%; the alcohol took up solid crystalline, and thin fluid fat, chlorides of sodium and potassium, lactates of soda and ammonia, extract of flesh, and traces of phosphate of lime. By washing the clot, 6% of fibrin were obtained. Hence, if we consider the fluid of the clot to be serum, we have the composition of this blood expressed as follows:

Water	.	.	.	.	740·00
Solid residue	.	.	.	.	260·00
Fibrin	.	.	.	.	11·00
Albumen	.	.	.	.	110·42
Blood-corpuscles	.	.	.	.	124·46
Extractive matters and salts	.	.	.	.	14·10

<sup>1</sup> London Medical Gazette, Jan. 1838.

<sup>2</sup> Ansell's Lectures on the Blood. The Lancet, 1840, p. 840.

<sup>3</sup> Poggendorf's Annalen, vol. 49, p. 328.



The blood-corpuscles, therefore, fall below Lecanu's average, while the albumen and solid constituents, generally, are considerably increased.

Lecanu<sup>1</sup> has made several experiments upon the quantity of solid constituents in the blood in cholera, and has arrived at the following results :

Solid constituents	. . . . .	340	251	520	330
Water	. . . . .	660	749	480	670

O'Shaughnessy<sup>2</sup> has analysed the serum of the blood in this disease, and has detected a considerable quantity of urea in it.

1000 parts were composed of,

Water	. . . . .	854·0
Albumen	. . . . .	133·0
Urea	. . . . .	1·4
Crystalline and fluid fat	. . . . .	1·4
Chlorides of sodium and potassium	. . . . .	4·0
Sulphates and muriates	. . . . .	1·6
Extractive matter and albuminate of soda	. . . . .	4·8

I analysed the blood of a woman labouring under a severe attack of sporadic cholera.

1000 parts of blood contained :

	Analysis 40.
Water . . . . .	750·530
Solid constituents . . . . .	249·470
Fibrin . . . . .	2·470
Fat . . . . .	5·434
Albumen . . . . .	114·114
Hæmatoglobulin . . . . .	108·529
Extractive matters and salts	10·631

The salts amounted to only 5·41, the average quantity being from 7 to 8 in 1000 parts of blood. We see that the water is decidedly diminished, but the ratio of the blood-corpuscles to the albumen is not such as was formerly supposed.<sup>3</sup> In consequence of the suppression of the urinary and biliary secretions, the blood contained a quantity of urea and of the constituents of the bile, (bilin and biliverdin.)

[Heller examined the blood taken after death from the carotids of a man who died of sporadic cholera.

<sup>1</sup> Etudes chimiques, etc., p. 106.

<sup>2</sup> Ancell's Lectures on the Blood. Lancet, 1840, p. 840.

<sup>3</sup> It was conceived that the thick and often imperfectly coagulated blood must be very rich in corpuscles, in consequence of the amount of serum thrown off by the intestinal canal.

It was of a very dark colour and of a tolerably thick consistency.

Under the microscope the blood-corpuscles appeared hacked at the edges, as if the capsules were partially destroyed, and many fat-vesicles were seen.

The blood was very rich in albumen, in fat, and in urea. The fixed salts, especially the chlorides, were increased,<sup>1</sup> and the fibrin appeared to be beneath the normal standard. There was no trace of biliphæin.]

## II. SUGAR IN THE BLOOD: MELITEMIA.

The blood in diabetes has been found by several observers, and in one instance by myself, to contain a larger proportion of solid constituents than healthy blood: others, as Lecanu and Henry, state that the amount is smaller. According to the latter, the quantity of blood-corpuscles is diminished, while others assert that they are increased. The fibrin remains at about the normal quantity. Rollo was, I believe, the first who proved the presence of sugar in the blood during diabetes. Gueudeville,<sup>2</sup> Vauquelin, Segalas,<sup>3</sup> Wollaston, Henry and Soubeiran, could not detect it. Bouchardat,<sup>4</sup> however, directs attention to the important consideration that the presence of sugar in the blood can only be incontestably proved when venesection has been performed two or three hours after dinner, and that if blood is drawn in the morning, no traces of it can be found: I have corroborated this observation.

I have analysed the blood in three cases of diabetes. The sugar was sought for in the manner described in page 185.

	Analysis 41.	Analysis 42.	Analysis 43.
Water . . . . .	794·663	789·480	802·000
Solid constituents . . . . .	205·337	210·510	198·000
Fibrin . . . . .	2·432	2·370	2·030
Fat . . . . .	2·010	3·640	2·250
Albumen . . . . .	114·570	86·000	97·450
Globulin . . . . .	66·300	98·500	74·350
Hæmatin . . . . .	5·425	5·100	3·700
Sugar . . . . .	2·500	a trace	a trace
Extractive matters and salts . . . . .	9·070	14·900	12·680

<sup>1</sup> In consequence of the torpidity of the urinary secretion.

<sup>2</sup> *Annal. de Chimie*, vol. 44, p. 45.

<sup>3</sup> *Journal de Chimie Médicale*, vol. 1, p. 1.

<sup>4</sup> *Revue Médic.* 1839, p. 321.

The blood in analysis 41 was obtained from a man aged 50 years, who had taken a full meal of animal food two hours previous to being bled. The 2·5 parts of sugar were not perfectly pure; they contained extractive matter, and some salts.

The blood in analysis 42 was taken before dinner from a girl aged 20 years. The presence of sugar was only just perceptible by the taste, by the sulphuric acid test, and by the odour evolved on burning it. The disease in this case was far advanced, and it is worthy of remark that, six or eight days previous to dissolution, the diabetes sapidus became converted into diabetes insipidus.

This patient made an extremely large quantity of water, which was not very abundant in sugar; while the man, aged 50, passed only two or three quarts of urine daily, containing a large proportion of sugar.

The blood in analysis 43 was taken before dinner from a man aged 30 years, who passed a very large quantity of water, which, however, did not contain much sugar.

I give, in the following table, the analyses of other observers:<sup>1</sup>

	Bouchardat.	Henry and Soubeiran.	Lecanu.
Water . . . . .	808·76	816·50	848·35
Solid constituents . . . . .	191·24	183·50	151·65
Fibrin . . . . .	1·95	2·43	
Albumen . . . . .	62·54	55·48	58·47
Blood-corpuscles . . . . .	118·25	120·37	85·18
Salts . . . . .	8·52	5·57	8·00

I further add the following analysis of the serum in diabetes, made by Rees.<sup>2</sup>

Water . . . . .	908·50
Albumen, with a trace of phosphate of lime and peroxide of iron . . . . .	80·35
Fat . . . . .	0·95
Diabetic sugar . . . . .	1·80
Alcohol-extract and urea . . . . .	2·20
Albuminate of soda, alkaline chlorides and carbonates, with a trace of sulphates and phosphates . . . . .	0·80

[Some very important additions to our knowledge of the pathology of this obscure disease will be found in Dr. Percy's 'Observations and Experiments concerning diabetes mellitus.' Med. Gaz. vol. ii, 1843.]

<sup>1</sup> In addition to those quoted in the text, there is an analysis of diabetic blood by Müller in the *Archiv d. Pharm.*, vol. 18, p. 55. Its extreme peculiarity renders its correctness doubtful.

<sup>2</sup> Ansell's Lectures on the Blood. The *Lancet*, 1840, p. 889.

## III. BILE-PIGMENT IN THE BLOOD: CHOLÆMIA.

Very contradictory statements exist regarding the composition of the blood in icterus.

Orfila<sup>1</sup> found bile, or at least, biliary resin, in the blood of three persons suffering from icterus; and Collard de Martigny<sup>2</sup> and Clarion<sup>3</sup> obtained similar results. Lassaigne<sup>4</sup> and Thenard,<sup>5</sup> on the contrary, declare that they could never detect any constituent of the bile in such cases. Chevreul found, in the blood of children with icterus, the colouring matter of the bile, but not picromel; and Boudet and Lecanu have likewise found the bile-pigment present in these cases.

I was fortunate enough to obtain a specimen of the blood of a woman in our hospital who was jaundiced to a degree not often witnessed. The skin over the whole body was of a yellowish brown colour, the urine was of a deep, dark brown tint, and deposited a considerable quantity of brown and yellow sediment. The blood was drawn from the arm in my presence, and was immediately whipt. It hardly differed in appearance from normal blood, but contained very little fibrin, and the corpuscles speedily sunk. The serum was of an almost blood-red colour, but, when only a thin stratum was viewed, it appeared of a bright amber tint. Its taste was hardly at all bitter; when treated with nitric acid, a whitish yellow coagulum was first formed, (consisting of albumen,) which rapidly assumed a deep grass-green colour, then, after a short interval, changed into a blue, and afterwards into a pale red; and from that to a yellow.

I precipitated the protein-compounds, by means of alcohol, from a large quantity of serum, evaporated the fluid, again treated the residue with alcohol, evaporated, and then dissolved the residue in water. This aqueous solution must have contained bilin or bilifellinic acid (if they had been present), besides the alcohol-extract of the blood and certain salts, but it neither tasted bitter, nor, when digested with sulphuric acid, did it yield a resinous substance (a compound of fellinic and cholinic acids

<sup>1</sup> *Eléments de Chim.*, vol. 2, p. 313.

<sup>2</sup> *Journ de Chim. Méd.*, vol. 3, p. 423.

<sup>3</sup> *Thèses d'Ecole de Médecine*, 1811.

<sup>4</sup> *Journ. de Chim. Méd.*, vol. 1, p. 266.

<sup>5</sup> *Traité de Chim.*, vol. 5, p. 111.



and dyslysin) ; neither did it contain bilin nor any of the products of its metamorphosis. On the other hand, I found, in the urine of this person, which was brown, very acid, and contained a large quantity of uric acid, a very appreciable quantity of biliary resin.

We can only account for the occurrence of this product of the metamorphosis of bilin in the urine, by recollecting the facility and rapidity with which noxious matters are eliminated from the blood.

My analysis of the blood in icterus gave the following results :

						Analysis 44.
Water	.	.	.	.	.	770·000
Solid residue	.	.	.	.	.	230·000
Fibrin	.	.	.	.	.	1·500
Fat	.	.	.	.	.	2·640
Albumen	.	.	.	.	.	126·500
Globulin	.	.	.	.	.	72·600
Hæmatin	.	.	.	.	.	4·840
Hæmaphæin, with biliphæin	.	.	.	.	.	2·640
Extractive matters and salts, with biliphæin	.	.	.	.	.	16·500

The peculiarities of this blood are, its large amount of solid constituents, due to an increase, not of the corpuscles, but of the albumen, the diminished quantity of fibrin, and the excess of colouring and extractive matters and salts. In other analyses of the blood I have frequently found it impossible to separate the hæmaphæin from the hæmatin, in consequence of the small amount of the whole colouring matter ; in this instance, however, I was able to effect their separation, and it appears that the amount of the hæmaphæin is about one half of that of the hæmatin, a proportion which is probably larger than occurs in healthy blood. The fat was not particularly increased.

The researches of Denis and Lecanu give, to a certain degree, similar results : they show a decrease of the blood-corpuscles, but not an increase of the solid constituents.

	Lecanu.		Denis.
	1.	2.	
Water	828·660	830·0	815·00
Solid constituents	171·340	170·0	185·00
Fibrin			9·50
Fat			6·00
Albumen	76·800	65·0	53·00
Blood-corpuscles	79·620	97·0	93·95
Salts			8·00
Yellow and blue pigment			14·55
Salts, extractive matters, and fat	14·900	8·0	

The large amount of fibrin and of fat is remarkable in Denis's analysis: the 1.45 parts of colouring matters were probably combined with extractive matter.

Tiedemann and Gmelin observed that the clot of icteric blood was of the ordinary colour. The clear yellow serum contained biliphæin, and gave, when treated with a small quantity of hydrochloric acid, a hyacinth-red colour, which, in the course of the night, became green; if an excess of acid was used, a hyacinth-red colour was at once produced, which, in the course of the night, turned to a blue. When treated with a quantity of nitric acid not sufficient to precipitate the albumen, it became of a greenish yellow colour; when treated with an excess of the acid, it gave a green precipitate, which afterwards became blue, and subsequently violet, red, and yellow.

[Becquerel and Rodier observe that, in icterus, there may be a continued secretion and flow of bile, or there may be perfect retention arising from biliary calculi, &c.

In the first case, no peculiar modification is observable in the blood, and it is, therefore, unnecessary to quote their analyses; in the second case, there is an accumulation of cholesterin and of the other fatty matters in the blood.

The following analysis was made of the blood of a young man, aged 23 years, in whom icterus was developed as a consequence of indigestion. There was constipation, and no appearance of bile in the fæces. The blood contained, in 1000 parts:

Water	.	.	.	.	740.509
Solid constituents	.	.	.	.	259.491
Fibrin	.	.	.	.	1.900
Fat	.	.	.	.	3.646
Albumen	.	.	.	.	66.300
Blood-corpuscles	.	.	.	.	164.300
Extractive matters and salts	.	.	.	.	23.345

The fatty matters amount to more than double the normal quantity, and consisted of:

Serolin	.	.	.	.	0.070
Phosphorized fat	.	.	.	.	0.810
Cholesterin	.	.	.	.	0.627
Saponified fat	.	.	.	.	2.139

The fatty acids that enter into the composition of the saponified fat occur in the bile, combined with soda. The salts were normal.

In another case of a similar nature, the fat amounted to 4·176, consisting of:

Serolin . . . .	0·128
Phosphorized fat . .	1·159
Cholesterin . . . .	0·556
Saponified fat . . . .	2·333

In addition to the large amount of fat in the blood in these cases, Becquerel and Rodier observed that the serum was always tinged with bile-pigment.]

#### IV. FAT IN THE BLOOD: PIARHÆMIA.

It is well known that free fat in the form of globules is not ordinarily seen in healthy human blood. The greater part exists in a saponified state, with the exception of cholesterin and serolin, which do not saponify with potash. As, however, the chyle contains a large quantity of free fat soon after the act of digestion, we must conclude that during the process of metamorphosis of the blood the greater part becomes converted into fatty acids. In certain pathological states of those organs which play an active part in the metamorphosis of the blood, and whose cells contain a considerable quantity of fat, as the liver and kidneys, and during inflammatory affections of the peritoneum and of the lungs, so large a quantity of both free and combined fat is sometimes found in the blood, that the serum appears turbid, opaque, and even milky.

Marcet found the serum milky in diabetes, Trail in hepatitis, Zanarelli in pneumonia, Christison in dropsy, icterus, and nephritis; moreover, in cholera the blood has been found to be very abundant in fat.

It is hardly necessary to observe that if in such cases the serum appear turbid, whey-like, or milky, fat-globules will be perceptible under the microscope.

Christison and Lecanu<sup>1</sup> have found that this, like most of the animal fats, consists of olein, margarin, and stearin: there is little doubt but that fatty acids are also present; in fact, Lassaigue detected a fat of this nature in the blood, similar to the fatty matter of the brain.

Zanarelli<sup>2</sup> found the blood of a man with pneumonia similar

<sup>1</sup> Etudes chimiques, p. 116.

<sup>2</sup> Journal de Chimie Médic., vol. 2, p. 551.

to milk : it separated into a thicker and a thinner portion. Blood taken some days afterwards separated into a red clot and into a milky serum. Zanarelli is of opinion that this milky blood is chyle, which has not been converted into proper blood, in consequence of the affection of the lungs. Bertazzi analysed it, and his results are given below.

*Bertazzi's Analysis of Milky Blood.*

Water . . . . .	905.0
Solid constituents . . . . .	95.0
Crystalline fat . . . . .	4.0
Non-crystalline fat . . . . .	6.0
Extractive matter, lactates, and chlorides . . . . .	5.0
Carbonates, phosphates, and sulphates . . . . .	4.0

Dr. Sion<sup>1</sup> observed an instance of milky blood in a case of mammary abscess. It contained no fibrin, and when allowed to stand a small quantity of colouring matter was deposited. The fluid was analysed by Lecanu, and the following are the results he obtained :

*Lecanu's Analysis of Milky Blood.*

Water . . . . .	794.0
Solid constituents . . . . .	206.0
Albumen . . . . .	64.0
Fat ; cholesterin, margarin, stearin, and fatty acids . . . . .	117.0
Salts and extractive matter . . . . .	25.0
Hæmatoglobulin . . . . .	a trace.

In a case of milky serum, which occurred during hepatitis, Trail found :

Water . . . . .	789
Albumen . . . . .	157
Oily fat . . . . .	45
Chlorides and lactates . . . . .	9

V. PUS IN THE BLOOD : PYOHÆMIA.

According to Gulliver,<sup>2</sup> pus is found, and probably is also formed, in the blood in all diseases in which there is suppuration, or even inflammatory swelling, accompanied with hectic fever. According to Blandin, blood of this nature, in issuing from the vein, does not differ much in appearance from ordinary blood ; it is frequently, however, rather darker and more fluid. When the blood is inflamed and purulent, a muddy or greenish

<sup>1</sup> Lancette franç. 1835, No. 49.

<sup>2</sup> Lond. and Edin. Phil. Mag. 1838.



yellow inflammatory coat is formed, in which, according to Piorry, gray granulations of a puriform appearance occur.

Ammonia has been recommended by Donn  as a test for the presence of pus in the blood. Blood treated with ammonia dissolves into a clear fluid, while pus similarly treated forms a stiff jelly. If, therefore, blood contains pus, it will become more or less gelatinous upon the addition of ammonia, and if only a very small quantity of pus is present, then we shall only find stripes of this stringy substance deposited at the bottom of the vessel. I have obtained favorable results from this method when the quantity of pus has not been very minute; I will not, however, venture to assert that certain results can be obtained by this method when the amount of pus is extremely small.

Gulliver,<sup>1</sup> Gluge,<sup>2</sup> and many others have availed themselves of the microscope for the detection of pus in the blood, and I am inclined to believe that this method gives the most certain results. The blood contains, in addition to its own corpuscles, the so-termed chyle-corpuscles, which are one half, or even quite, as large again as the blood-corpuscles. They do not possess the yellow colour of the latter; they are gray, only slightly granular, and possess a sharp, dark, circumscribed edge; their rolling motion, on inclining the stage of the microscope, shows that they are perfectly spherical, and they do not, like the blood-corpuscles, dissolve in water. If, however, the chyle-corpuscles remain in contact with water for some time (from half an hour to an hour), they undergo a change; they increase a little in size, become clearer, their edge appears less sharp, their shape is no longer spherical, but oblong or irregular, and they become more distinctly granular, or else dark points become apparent in the interior, as indications of nuclei. In this condition the chyle-corpuscles may be easily mistaken for pus-corpuscles; the latter are, however, usually rather larger than the tumefied chyle-corpuscles, and they are paler, their edge is granular, or tuberculated, and often very uneven, their shape is round, or oblong, occasionally irregular, and they appear slightly granular in the interior, indicating from three to five nuclei. In very many cases we see two, three, five, or even more pus-cor-

<sup>1</sup> Op. cit.

<sup>2</sup> Fragmente zur Pathologie des Blutes. Anatomisch-Mikroskopische Untersuchungen. Heft 1. 1839.

puscles lying closely attached to each other, while the chyle-corpuscles almost always swim about separately. By this means I have recognized pus in the blood, both when it has been artificially placed there, and on analysing the blood which I took from the inflamed vein of a person who had died from phlebitis.

In one instance, in which I found a considerable quantity of pus in the blood, taken from the inflamed vein in a case of traumatic phlebitis, I could detect no traces of pus in the blood taken from the vena cava and from the heart.

This is all that I can state from my own experience regarding the detection of pus in the blood.

#### VI. ANIMALS IN THE BLOOD.

Early authors speak of living animals in the blood. Dr. Chiaje,<sup>1</sup> of Naples, has recently stated that he found the polystoma sanguiculum in the expectorated blood of two phthisical patients who were attacked with hæmoptysis. Some of these small flat worms, which are similar to leeches, were floating about in the serum, others attached themselves to the sides of the vessel. Chiaje characterizes the polystoma in the following terms: "*Corpus teretiusculum, seu depressum, pori sex antici ventrales, et posticus solitarius; habitat in venoso systemate hominis, et præsertim in ejusdem pulmonali parenchymate.*"

[Dr. Goodfellow has lately recorded a case in which an immense number of animalculæ were found in the blood of a fever-patient. They varied in length from 1-5000th to 1-3000th of an inch, and in diameter, which was the same throughout, from 1-40,000th to 1-20,000th of an inch. A singular case was observed by Mr. Bushman, in which worms of about half an inch in length were found in the blood of a boy labouring under influenza.—Ansell's Lectures on the Blood. 'Lancet,' 1840, p. 778.]

#### SUPPLEMENT.

The following analyses of the blood of a pregnant woman (in her fifth month), and of menstrual blood, could not be naturally inserted among either of our four forms of diseased blood, and will find a proper place in a supplement.

<sup>1</sup> Omodei, *Annali universal.*, Oct. 1837.

The blood of the pregnant woman formed a slight buffy coat, but otherwise differed in no respect physically from normal blood.

It was composed of :

				Analysis 45.
Water	.	.	.	806.898
Solid constituents	.	.	.	193.102
Fibrin	.	.	.	2.102
Fat	.	.	.	3.040
Albumen	.	.	.	72.200
Hæmatoglobulin	.	.	.	96.900
Extractive matters and salts	.	.	.	7.980

The chief point of difference between this and normal blood is that, in this case, the amount of solid constituents is somewhat below the standard. The proportion of the hæmatoglobulin to the albumen is normal ; the quantity of fat is rather increased.

[Becquerel and Rodier analysed the blood of nine pregnant women, viz. one at the fourth month, five at the fifth month, one at five months and a half, one at six months, and one at seven months.

The maxima, minima, and mean results are given in the following table :

	Mean.	Max.	Min.
Density of defibrinated blood . . . . .	1051.5	1055.1	1046.2
Density of serum . . . . .	1025.5	1026.8	1023.6
Water . . . . .	801.6		
Fibrin . . . . .	3.5	4.0	2.5
Albumen . . . . .	66.1	68.8	62.4
Blood-corpuscles . . . . .	111.8	127.1	87.7
Extractive matters and salts . . . . .	6.6	8.7	4.7
Fat . . . . .	1.922	2.519	1.158
Consisting of—Serolin . . . . .	variable	0.108	0.018
Phosphorized fat . . . . .	0.646	0.863	0.381
Cholesterin . . . . .	0.061	0.225	0.030
Saponified fat . . . . .	1.195	1.323	0.737

The salts in 1000 parts of blood consisted of :

Chloride of sodium . . . . .	3.2	3.9	2.3
Other soluble salts . . . . .	2.4	2.8	1.8
Phosphates . . . . .	0.425	0.690	0.282
Iron . . . . .	0.449	0.490	0.370

From these analyses they conclude that pregnancy exercises a marked influence on the composition of the blood. The density both of the defibrinated blood and of the serum is

diminished, the water, the fibrin, and the phosphorized fat<sup>1</sup> are increased, while the corpuscles and the albumen are diminished.]

The menstrual blood was obtained at a period at which it contained no epithelium scales. It did not coagulate; it contained some vaginal mucus, but it was not putrid nor of an unpleasant smell.

It was composed of:

	Analysis 46.
Water . . . . .	785·000
Solid constituents . . . . .	215·000
Fat . . . . .	2·580
Albumen . . . . .	76·540
Hæmatoglobulin . . . . .	120·400
Extractive matters and salts . . . . .	8·600

The most striking peculiarities of this blood are, the total absence of fibrin, and the increase of the solid constituents caused by the excess of the blood-corpuscles. The hæmatoglobulin was found to be very rich in hæmatin, combined, undoubtedly, with a considerable amount of hæmaphæin; the colouring matter amounted to 8·3% of the hæmatoglobulin.

[In an analysis made by Denis, and quoted by Raciborski in his Essay on Menstruation, (in l'Expérience, No. 333,) the menstrual fluid was found to consist of:

Water . . . . .	825·0
Solid constituents . . . . .	175·0
Fibrin . . . . .	0·5
Phosphorized fat . . . . .	3·9
Albumen . . . . .	48·3
Blood-corpuscles . . . . .	63·4
Mucus . . . . .	45·3
Osmazome and cruorin . . . . .	1·1
Soluble salts . . . . .	9·5
Earthy phosphates and carbonates . . . . .	2·5
Peroxide of iron . . . . .	0·5

Rindskopf analysed the menstrual discharge of a vigorous and healthy girl. It was extremely acid, and contained:

1st Analysis.		2d Analysis.	
Water . . . . .	820·830	Water . . . . .	822·892
Solid residue . . . . .	179·170	Albumen and hæmatoglobulin . . . . .	156·457
Salts . . . . .	10·150	Extractive matters and salts . . . . .	20·651

<sup>1</sup> The phosphorized fat is always abundant in impoverished blood.



Vogel analysed the menstrual discharge in a case of prolapsed uterus. It was of an intensely red colour, thick, and viscid ; it did not coagulate, but, after standing for some time, a colourless serum separated. The fluid obtained at the commencement of the flux yielded 83·9 parts of water and 16·1 of solid materials, and that obtained near the termination yielded 83·7 of water and 16·3 of solid materials. The serum contained 93·53 parts of water and 6·47 of solids, of which 0·64 were fixed salts. There can be little doubt that there is fibrin in the menstrual secretion ; its determination is, however, usually rendered impossible by the presence of a large amount of mucus, which seems to deprive the blood of its power of coagulating.

*Lochial discharge.* Scherer has carefully investigated this subject. The following is a summary of his results.

During the first day the discharge was of a brownish red colour, viscid, formed no coagulum, but, when collected in a vessel, threw down a slimy deposit, consisting of normal blood-corpuscles, with which a few partially-dissolved and broken-up corpuscles, together with mucus-corpuscles and epithelium scales were interspersed. The supernatant serum was clear and yellow, and the microscope revealed in it a large number of fat-vesicles. It was devoid of odour, perfectly neutral, and contained in 1000 parts :

Water . . . . .	740
Solid constituents . . . .	260

On the second day there were still blood-corpuscles, but they were fewer and less perfect, most of them being irregular and indentated at the edges ; there were mucus-corpuscles and epithelium scales, but in less number than on the preceding day. The fluid still deposited a viscid sediment, but the serum was more highly coloured than on the previous day. The reaction was neutral ; there was a faint odour. 1000 parts consisted of:

Water . . . . .	812·2
Solid constituents . . . .	187·8

The residue, on incineration, yielded 9·35 of alkaline ferruginous ash.

On the third day the secretion resembled arterial blood. The blood-corpuscles were, for the most part, perfect, and normal mucus-corpuscles were observed.

In 1000 parts there were :

Water . . . . .	760
Solid constituents . . . . .	240

The ash amounted to 12·2. There was an appreciable quantity of fibrin in this day's secretion, arising possibly from a slight hæmorrhagic effusion.

On the fourth day the secretion was of a dirty brown colour, the corpuscles were more or less injured, and there was a distinct odour of ammonia. There were numerous mucus-corpuscles, but no epithelium. 1000 parts yielded 191 of solid residue, and 9·5 of alkaline salts.

On the fifth day the discharge was of a greenish yellow colour ; it contained very few blood-corpuscles, most of which were more or less injured, but numerous mucus-corpuscles arranged in groups of 5—10 together. The reaction of the fluid was alkaline, there was a strong odour of ammonia, and 1000 parts yielded 93·5 of solid residue.

On the sixth day the fluid was of a brown colour, smelled like putrid cheese, and developed ammonia freely. 1000 parts gave 76 of solid residue. For other analyses and further information on this subject the reader is referred to 'Scherer's *Chemische und Mikroskopische Untersuchung zur Pathologie.*' Heidelberg, 1843.]

#### *Blood of animals.*

In addition to the 12 analyses of horse's blood which have already appeared, I may communicate the three following :

	Analysis 47.	Analysis 48.	Analysis 49.
Water . . . . .	800·562	818·900	808·809
Solid constituents . . . . .	199·437	182·100	191·191
Fibrin . . . . .	4·747	5·100	9·011
Fat . . . . .	5·149	2·214	4·820
Albumen . . . . .	62·276	62·140	103·740
Hæmatoglobulin . . . . .	100·291	96·100	58·960
Extractive matters and salts	12·454	12·310	14·650

The blood in all these analyses was taken from horses suffering from malleus humidus. Analyses 48 and 49 refer to the same horse, but in the latter case the animal was kept for four days without food, being merely allowed water during that period. Taking into consideration the deprivation of nutriment,

we cannot help feeling surprised at the large amount of solid constituents that occur in this analysis; it can only be explained by supposing that a larger amount of fluid was removed from the blood by secretion and excretion than was supplied to it by the drink. Another peculiarity is the increase of fibrin and of fat, and the diminution of blood-corpuscles; this change may, however, be readily explained, for as long as the organs of respiration, secretion, and excretion, continue to discharge their functions, the blood must obviously be changed by them, and this change will especially affect the corpuscles. The horse passed little urine during this time, but this little was tolerably saturated. It was by no means strong at the commencement of the experiment, but at its termination it was much exhausted, and the respiration became gasping. The blood formed a very strong inflammatory crust.

The blood of a healthy ox,<sup>1</sup> and of a healthy calf, yielded the following results:

	Analysis 50.	Analysis 51.
Water . . . .	795·000	777·279
Solid constituents . .	205·000	222·721
Fibrin . . . .	—	2·600
Fat . . . .	5·590	4·191
Albumen . . . .	95·050	83·925
Hæmatoglobulin . .	91·710	105·925
Extractive matters and salts	11·181	24·444

In the former of these analyses, the fluid which was examined, was a mixture of arterial and venous blood, from which the fibrin had been previously removed: in the latter case the extractive matter was not separated from hæmatin. The number 105·925 represents the globulin perfectly free from colouring matter.

[Andral, Gavarret, and Delafond, have published a valuable essay on the blood of some of our domestic animals in health and disease. They made no less than 222 analyses of the blood of 155 animals, viz. 41 analyses of the blood of dogs, 31 of horses, 110 of sheep, 2 of goats, 23 of oxen and cows, and 7 of swine.

<sup>1</sup> Berzelius (Thierchemie, p. 98) found, in the serum of the blood of oxen—water 905, albumen 80, albuminate of soda and lactate of potash 6·2, chloride of potassium 2·6, and modified albumen with carbonate and phosphate of potash 1·5.

In order to give an idea of the composition of the blood in the different species of animals, we shall communicate the average, maxima, and minima numbers that were obtained. For the principles on which the analyses are founded, see p. 241. Analyses of the blood of 17 horses gave the following results:

	Fibrin.	Blood-corpuscles.	Residue of serum.	Water.
Mean . .	4.0	102.9	82.6	810.5
Maximum .	5.0	112.1	91.0	833.3
Minimum .	3.0	81.5	74.6	795.7

Analyses of the blood of 14 neat cattle yielded:

	Fibrin.	Blood-corpuscles.	Residue of serum.	Water.
Mean . .	3.7	99.7	86.3	810.3
Maximum .	4.4	117.1	93.6 (?)	824.0
Minimum .	3.0	85.1	82.9	799.0

The mean results of the blood of 6 bulls (1), and of an equal number of milch cows (2), indicated no important differences.

	Fibrin.	Blood-corpuscles.	Residue of serum.	Water.
(1.) . .	3.6	97.4	85.8	813.2
(2.) . .	3.8	101.9	86.8	807.5

Analyses of the blood of 6 swine of the English breed yielded:

	Fibrin.	Blood-corpuscles.	Residue of serum.	Water.
Mean . .	4.6	105.7	80.1	809.6
Maximum .	5.0	120.6	88.7	816.9
Minimum .	4.1	92.1	73.6	793.9

The blood of 2 goats gave:

	Fibrin.	Blood-corpuscles.	Residue of serum.	Water.
Mean . .	3.2	101.4	91.4	804.0
Maximum .	3.5	105.7	92.0	809.2
Minimum .	2.6	97.2	90.8	798.8

Sheep of various breeds appeared to differ slightly in the composition of the blood.

Analyses of the blood of 19 sheep of the Rambouillet<sup>1</sup> breed yielded:

	Fibrin.	Blood-corpuscles.	Residue of serum.	Water.
Mean . .	3.1	98.1	83.5	815.3
Maximum .	3.8	109.6	96.6	830.3
Minimum .	2.6	82.5	74.7	808.7

The blood of 11 sheep of a crossed variety, (the Naz-Rambouillet breed,) yielded:—

<sup>1</sup> A variety of the Merino sheep.



	Fibrin.	Blood-corpuscles.	Residue of serum.	Water.
Mean . .	2·8	106·1	80·3	810·8
Maximum .	3·4	123·4	87·7	827·2
Minimum .	2·3	94·6	74·7	789·8

The mean results from the blood of these 30 sheep were :

Fibrin.	Blood-corpuscles.	Residue of serum.	Water.
3·0	101·1	82·4	813·5

The blood of 13 English sheep yielded somewhat different results:

	Fibrin.	Blood-corpuscles.	Residue of serum.	Water.
Mean . .	2·6	95·0	92·4	810·0
Maximum .	3·3	110·4	97·0	822·1
Minimum .	2·0	83·8	82·6	795·3

From the blood of 16 dogs<sup>1</sup> they obtained :

	Fibrin.	Blood-corpuscles.	Residue of serum.	Water.
Mean . .	2·1	148·3	75·5	774·1
Maximum .	3·5	176·6	88·7	795·5
Minimum .	1·6	127·3	60·9	744·6

The blood was found to offer considerable differences in breeding animals before and after delivery :

	Fibrin.	Blood-corpuscles.	Residue of serum.	Water.
Sheep 36 hours before delivery .	2·3	95·0	81·7	821·0
„ 66 hours after delivery .	3·0	106·2	78·2	812·6
„ 24 hours before delivery .	2·9	92·9	84·5	819·7
„ 72 hours after delivery .	3·5	102·6	86·3	807·6
Cow 5 days before delivery .	3·7	90·9	75·2	830·2
„ 2 days after delivery .	5·1	98·8	73·7	822·4

That the blood of the lamb differs considerably from the blood of the parent sheep, is obvious from the following analyses:

	Fibrin.	Blood-corpuscles.	Residue of serum.	Water.
Male lamb, aged 3 hours . .	1·9	108·6	63·3	826·2
„ 24 hours . .	1·9	117·0	74·2	806·9
„ 48 hours . .	2·5	103·3	80·7	813·5
„ 96 hours . .	3·0	109·1	68·6	819·3

The maxima, minima, and average numbers quoted above, are sufficient to prove that the blood of different species of animals varies in its composition from that of man and of each

<sup>1</sup> Gmelin (Handbuch der theoretischen Chemie, vol. 2, p. 1387) found, in the arterial blood of a dog—water 898, and fibrin 2·09; the dried serum contained, albumen 88·3, and salts 11·7; the venous blood contained, water 843, and fibrin 2·1; the dried residue of the serum consisting of albumen 87·5, and salts 12·5.

other. This is a point of no slight importance, for it indicates the necessity that exists for the determination of the constitution of the healthy blood in every individual class of animals before we can venture to draw any conclusions regarding the blood in a morbid state.

The mean amount of fibrin in one class of animals is as low as 2.1, while in another it rises to 4.6 per mille, one being considerably lower, the other much higher, than in man.

The largest amount of fibrin observed by Andral, Gavarret, and Delafond, was in swine, the maximum being 5.0, and the minimum 4.1; the animals were from 2 to 6 months old, and had been restricted for some time to a diet of horse-flesh. In a two-year old sow that had been fed purely on vegetables, and was very fat, the fibrin did not exceed 4.0. The blood of horses ranks next to that of swine in the amount of fibrin, the observed mean being 4.0, the maximum 5.0, and the minimum 3.0. Next to horses come neat cattle, the mean amount of fibrin in their blood being 3.7, the maximum 4.4, and the minimum 3.0. The blood of the bull does not contain a larger amount of fibrin than the blood of the cow or the ox. The blood of the Merino sheep contains on an average the same amount of fibrin as human blood,<sup>1</sup> namely, 3.0; in the blood of English sheep a smaller amount of fibrin was obtained. The smallest quantity of fibrin was found in the blood of dogs, the mean being only 2.1, the maximum 3.5, and the minimum 1.6. The minimum occurred in dogs feeding on an exclusive animal diet. From these observations it is evident that each class of animals contains in its blood its own standard amount of fibrin. The blood-corpuscles are found to occur, for the most part, in an inverse ratio to the fibrin; that is to say, in blood that contains a large amount of fibrin, the amount of the corpuscles is small, and *vice versâ*. It was shown by special experiments that there is no connexion between the strength of the animal and the amount of fibrin. The amount of fibrin varies considerably before delivery and immediately afterwards, during the milk-fever; in the former case it is at its minimum, in the latter it attains its maximum.

The amount of solid residue of the serum varies between 75.5 and 92.4. The former number occurs in the blood of the

<sup>1</sup> Andral and Gavarret always refer to Lecanu's standard.

dog; the blood of swine, oxen, and Merino sheep, contains from 80·0 to 86·0, and the maximum occurs in the blood of the English sheep.

The investigations of these chemists relating to the blood of domestic animals in a morbid state, were principally confined to sheep suffering from watery cachexia.<sup>1</sup> We extract the following analyses from their essay, as illustrative of the changes that the blood undergoes in pure hydræmia without any complication.

		Fibrin.	Blood-corpuscles.	Residue of serum.	Water.
A 5-year old sheep:	1st Venesection	. 3·1	44·8	52·7	899·4
"	2d "	. 3·0	42·2	50·9	903·9
A 6-year old sheep:	1st "	. 3·5	46·7	69·5	880·3
"	2d "	. 3·5	46·6	70·7	879·2
A 6-year old sheep:	1st "	. 2·8	49·1	59·1	889·0
"	2d "	. 2·6	42·4	55·9	899·1
"	3d "	. 2·9	40·1	58·1	898·1
"	4th "	. 2·8	67·7	66·6	862·9
A 5-year old sheep:	1st "	. 2·4	39·4	63·4	894·8
"	2d "	. 2·3	33·3	55·8	908·6
"	3d "	. 3·0	29·3	52·1	915·6
"	4th "	. 3·0	14·2	51·9	930·9

The sheep, whose blood formed the subject of the last analyses, died shortly after the 4th venesection.

In those cases in which the hydræmia was associated with inflammatory affections, the blood presented very different characters, as the following analyses will show:

		Fibrin.	Blood-corpuscles.	Residue of serum.	Water.
A 5-year old sheep:	1st Venesection	. 9·6	32·9	79·1	878·4
"	2d "	. 6·4	30·0	78·6	885·0
A 4-year old sheep:	1st "	. 12·6	39·5	94·1	853·8
"	2d "	. 10·4	34·2	89·1	866·3
"	3d "	. 8·7	25·3	92·3	873·7
A 4-year old sheep:	1st "	. 5·7	60·1	99·1	835·1
"	2d "	. 4·3	54·6	95·9	845·2

The first of these animals had, in addition to the hydræmia, pneumonia and pulmonary abscess; the second, acute hepatitis and peritonitis; and the third, acute bronchitis.

The following analyses of the blood of sheep, with various disorders, were made by the same chemists:

<sup>1</sup> Commonly known as the rot.

	Fibrin.	Blood-corpuseles.	Residue of serum.	Water.
Sheep with acute bronchitis . . .	5·2	61·0	109·4	824·4
Ram with softened tubercles . . .	4·4	88·8	101·8	805·0
Sheep with tubercular pulmonary cavity .	6·2	64·5	106·7	822·6
Ram with acute enteritis . . .	6·0	100·7	96·6	796·7
Ewe with acute metritis . . .	6·3	100·4	85·4	807·9
Sheep with chronic peritonitis: 1st Venes.	3·3	63·2	57·6	875·9
"          "          2d      "	3·2	58·8	52·2	885·8
"          "          3d      "	3·1	52·8	52·6	891·5

They remark that the changes which the blood of these animals undergoes in disease, precisely correspond with those of human blood in similar disorders. Thus, in inflammatory diseases, there is always an excess of fibrin, and they observe that in those animals in which the normal mean amount is highest, the fibrin is increased in the greatest proportion; thus in the blood of a cow with inflammation of the respiratory organs, the fibrin rose to 13·0, the normal amount in that animal being 3·8. In dogs that were reduced to a very anæmic condition, the blood-corpuseles fell from the normal mean 1·48, to 104, and even down to 83.

Their attention was, however, principally directed to the watery cachexia, or rot in sheep. The most prominent phenomena of the disease were extreme debility, paleness of the mucous membranes, and very frequently serous infiltration of the conjunctiva, and of the cellular tissue of the integument of the feet. No albumen was detected in the urine. From 27 analyses made with the blood of 11 sheep, they conclude that the amount of fibrin is slightly affected, but that the blood-corpuseles are excessively diminished; from 78, their normal average, they fall to 40, 25, and even 14. The solid residue of the serum is diminished, (a point in which this disease differs from chlorosis in the human subject,) and the water is considerably increased.

The deficiency in the amount of blood-corpuseles appeared to vary with the progressing weakness of the animal. By proper food, and due attention to atmospheric influences, the corpuseles were observed to increase; in one instance they rose from 49 to 64.

From 14 analyses of the blood, in which this affection was associated with inflammatory disorders, it appeared that the



fibrin increases, and the blood-corpuscles diminish, as in simple, uncomplicated inflammations.

Lastly, they observed that when venesection was frequently had recourse to in inflammatory affections, each venesection tended to increase the amount of fibrin and of water, and to diminish the quantity of blood-corpuscles.

The following are the results of the first and last venesections of a horse that was bled seven times in 24 hours:

	Fibrin.	Blood-corpuscles.	Residue of serum.	Water.
The 1st Venesection gave .	3·1	104·0	90·8	802·1
7th        ,,        .	7·6	38·3	60·1	894·2

Nasse has likewise taken up this subject since the publication of Simon's Chemistry.

In the following analyses, which are extracted from his paper, the extractive matters of the blood and the insoluble salts appear to be included with the albumen:

	Water.	Fibrin.	Fat.	Blood-corpuscles.	Albumen.	Soluble salts.
Dog . .	790·50	1·93	2·25	123·85	65·19	6·28
Cat . .	810·02	2·42	2·70	113·39	64·46	7·01
Horse . .	804·75	2·41	1·31	117·13	67·85	6·82
Ox . .	799·59	3·62	2·04	121·86	66·90	5·98
Calf . .	826·71	5·76	1·61	102·50	56·41	7·00
Goat . .	839·44	3·90	0·91	86·00	62·70	7·04
Sheep . .	827·76	2·97	1·16	92·42	68·77	6·91
Rabbit . .	817·30	3·80	1·90	170·72		6·28
Swine . .	768·94	3·95	1·95	145·35	72·78	6·74
Goose . .	814·88	3·46	2·56	121·45	50·78	6·87
Hen . .	793·24	4·67	2·03	144·75	48·25	6·97

The following table represents the composition of the soluble and insoluble salts occurring in 1000 parts of the blood of these animals:

	<i>Soluble salts:</i>			
	Alkaline phosphates.	Alkaline sulphates.	Alkaline carbonates.	Chloride of sodium.
Dog . .	0·730	0·197	0·789	4·490
Cat . .	0·607	0·210	0·919	5·274
Horse . .	0·844	0·213	1·104	4·659
Ox . .	0·468	0·181	1·071	4·321
Calf . .	0·957	0·269	1·263	4·864
Goat . .	0·402	0·265	1·202	5·176
Sheep . .	0·395	0·348	1·498	4·895
Rabbit . .	0·637	0·202	0·970	4·092
Swine . .	1·362	0·189	1·198	4·281
Goose . .	1·135	0·090	0·824	4·246
Hen . .	0·945	0·100	0·350	5·392

The insoluble salts were found by Nasse to be combinations of peroxide of iron, lime, magnesia, silica, and phosphoric and sulphuric acids. The magnesia and silica were not determined quantitatively.

In 1000 parts of blood there were :

<i>Insoluble salts :</i>				
	Peroxide of iron.	Lime.	Phosphoric acid.	Sulphuric acid.
Dog . . .	0·714	0·117	0·208	0·013
Cat . . .	0·516	0·136	0·263	0·022
Horse . . .	0·786	0·107	0·123	0·026
Ox . . .	0·731	0·098	0·123	0·018
Calf . . .	0·631	0·130	0·109	0·018
Goat . . .	0·641	0·110	0·129	0·023
Sheep . . .	0·589	0·107	0·113	0·044
Swine . . .	0·782	0·085	0·206	0·041
Goose . . .	0·812	0·120	0·119	0·039
Hen . . .	0·743	0·134	0·935	0·010

The only animals in a state of disease whose blood was analysed by Nasse were sheep with chronic rot (hydræmia or watery cachexia), and horses with the glanders. The blood of three sheep affected with the disease in question gave the following results :

	A.	B.	C.
Water . . .	952·00	932·30	916·00
Fibrin . . .	2·75	3·84	3·90
Fat . . .	0·23	0·25	0·30
Blood-corpuscles . .	10·20	23·40	31·25
Albumen . . .	27·52	32·02	39·45
Soluble salts . . .	7·30	8·19	7·10

The sheep A was very much reduced, and the blood had much the appearance of reddened serum. There was effusion into the peritoneum. The sheep B was pregnant, and in bad condition ; while the sheep C had been delivered about 10 weeks previously, and had been since attacked with dropsy. The salts were determined individually, but they presented no peculiar deviation from the normal standard.

The following analyses refer to the blood of two horses A and B, suffering from chronic ozæna (the glanders) :

A.			B.	
1.	2.	3.	1.	2.
Water . . .	833·00	860·00	842·00	859·00
Fibrin . . .	8·90	7·50	6·60	8·70
Blood-corpuscles . .	65·50	43·30	68·20	44·20
Albumen and fat . .	86·58	83·68	76·70	82·27
Soluble salts . . .	6·02	5·52	6·50	5·38

The individual salts did not differ in any remarkable degree from the normal standard.

We have already had occasion to refer to the labours of Enderlin, in connexion with the chemistry of the blood. He has recently published the following analyses of the ash of the blood of various animals, which are confirmatory of the views to which we have more than once alluded, respecting the non-existence of lactates in the blood.

The analyses are calculated for 100 parts of ash :

*Salts soluble in water :*

	Ox.	Calf.	Sheep.	Hare. <sup>1</sup>
Tribasic phosphate of soda ( $3\text{NaO}, \text{PO}_5$ )	16.769	30.180	13.296	28.655
Chloride of sodium . . . .	59.340	52.650	66.570	50.324
Chloride of potassium . . . .	6.120			
Sulphate of soda . . . . .	3.855	2.936	5.385	3.721

*Salts insoluble in water :*

Phosphates of lime and magnesia . . . .	4.190	3.490	13.920	16.509
Peroxide of iron and phosphate of ditto	8.277	9.277		
Sulphate of lime, and loss . . . . .	1.449		0.829	

The alkaline carbonates in Nasse's analyses are easily accounted for by Enderlin's explanation of the action of the atmosphere on the tribasic phosphate of soda.]

I have analysed the blood of the carp and of the tench. In both fishes it was tolerably clear, contained oil-globules visible to the naked eye, formed a loose gelatinous clot, from which scarcely any serum separated, and yielded, on whipping, a viscid sort of fibrin, possessed of little tenacity, and which, on the addition of water, separated into minute flocculi, consisting (according to microscopic investigation) of granular masses and of minute vesicles far smaller than the nuclei of the blood-corpuscles. The blood coagulated imperfectly on boiling, and was remarkable for its small amount of hæmatoglobulin. The blood of *bufo variabilis* presented exactly similar phenomena; but on a chemical examination it was found to be richer in solid constituents, especially in albumen, than the blood of fishes. It was impossible to form a quantitative determination of the fibrin or of the colouring matter in the blood of these animals, in

<sup>1</sup> In another analysis he found bibasic phosphate of soda.

consequence of the aplastic character of the former constituent, and the minute quantity of blood that could be obtained.

The analyses gave :

	Analysis 52.	Analysis 53.	Analysis 54.
	Carp's blood.	Tench's blood.	Blood of <i>bufo variabilis</i> .
Water . . . . .	872·000	900·000	848·200
Solid constituents . . . .	128·000	100·000	151·800
Fibrin . . . . .	a trace	a trace	a trace
Fat . . . . .	2·967	4·670	9·607
Albumen . . . . .	83·850	68·800	112·330
Hæmatoglobulin . . . .	24·635	15·650	29·753
Extractive matters and salts .	6·129	2·770	2·429

On boiling the dried residue of the blood with spirit, after the removal of the fat, I obtained tinctures of a deep red colour, such as would have been yielded by the blood of the mammalia, but they differed in this respect, that they did not become turbid on cooling, and the hæmatoglobulin, instead of being deposited in flocks, had to be determined by evaporation. As the flesh of these animals differs from that of the mammalia, it is by no means impossible that there are corresponding differences in the globulin and hæmatin. The large amount of albumen in the blood of *bufo variabilis* may perhaps be attributed to the unavoidable mixture of the blood with lymph, and perhaps with mucus.

Dumas and Prevost analysed the blood of numerous animals. The blood was allowed to coagulate, the clot and serum were separately dried, and the serum that remained entangled in the clot was deducted, and added to the serum that spontaneously separated. The fibrin was not determined.

	Water.	Solid constituents.	Blood-corpuscles.	Residue of serum.
Ape: Simia Callitriche	776·0	224·0	146·1	77·9
Dog . . . . .	810·7	189·3	123·8	65·5
Cat . . . . .	795·3	204·7	120·4	84·3
Horse . . . . .	818·3	181·7	92·0	89·7
Calf . . . . .	826·0	174·0	91·2	82·8
Sheep . . . . .	829·3	170·7	93·5	77·2
Goat . . . . .	814·6	185·4	102·0	83·4
Rabbit . . . . .	837·9	162·1	93·8	68·3
Guineapig . . . . .	784·8	215·2	128·0	87·2
Raven . . . . .	797·0	203·0	146·6	56·4
Heron . . . . .	808·2	191·8	132·6	59·2
Duck . . . . .	765·2	234·8	150·1	84·7
Hen . . . . .	779·9	220·1	157·1	63·0



	Water.	Solid constituents.	Blood-corpuscles.	Residue of serum.
Pigeon . . .	797·4	202·6	155·7	46·9
Trout . . .	863·7	136·3	68·8	72·5
Eelpout . . .	886·2	113·8	48·1	65·7
Eel . . .	846·0	154·0	60·0	94·0
Land-tortoise . .	778·8	221·2	150·6	80·6
Frog . . .	884·6	115·4	69·0	46·4

[We have already alluded to the occurrence of animalcules in human blood: in the blood of the lower animals such cases are very frequently observed.

Cercaria have been discovered in the blood by Mayer, and in his 'Dissertatio de Organo Electrico et de Hæmatorosis; Bonn. 1843,' he mentions the following: (1,) Paramœcium loricatum s. costatum, in frogs; (2,) Amœba rotatoria in fishes.<sup>1</sup> Polystoma-like animalcules were described by Schmitz as occurring in the blood of the horse. (Dissertatio de Vermibus in Sanguine. Berol. 1826.)

Gruby and Delafond have described a peculiar animalcule of frequent occurrence in the blood of the dog, and numerous observers have noticed similar phenomena in the blood of the horse and the ass.]

### *The Lymph.*

Our knowledge of the chemical characters of the lymph is very deficient. It is described as a viscid yellow, greenish yellow, and occasionally red fluid, devoid of odour, possessing a slightly saltish taste, an alkaline reaction, and containing from 3 to 5·7% of solid constituents. The lymph of the human subject is described by Müller, Wurtzer, and Nasse as clear and of a yellow colour, while others assign to it the same tint, but assert that it is opalescent. It coagulates in the course of 10 or 15 minutes into a clear, tremulous, colourless jelly, and deposits an arachnoidal coagulum of fibrin, which was previously held in solution, as in the liquor sanguinis, and is usually colourless, although Tiedemann and Gmelin have observed it of a reddish tint. The fluid left after coagulation is rather thick, resembles almond oil in appearance, and under the microscope exhibits, even when perfectly clear, a number of colour-

<sup>1</sup> Valentin (Müller's Archiv, 1841, p. 436,) frequently detected this animalcule in the blood of the salmon, and once met with it in the fluid of the cerebral ventricles.

less corpuscles, apparently smaller than human blood-corpuscles, and far less numerous in it than the blood-corpuscles are in the blood. (Müller.) In addition to albumen, the serum of the lymph contains extractive matters and salts: the latter are the same as the salts of the blood.

Gmelin found in 1000 parts of human lymph:

Water	961.0
Solid constituents	39.0
Fibrin	2.5
Albumen	27.5
Chloride of sodium, phosphates of potash and soda, and salivary matter	2.1
Extractive matters and lactate of soda	6.9

Marchand and Colberg have analysed lymph obtained from a wound on the dorsum of a man's foot. They found in it:

Water	969.26
Solid constituents	30.74
Fibrin	5.20
Albumen	4.34
Extractive matter	3.12
Fluid and crystalline fat	2.64
Chlorides of sodium and potassium, alkaline sulphates and carbonates, sulphate and phosphate of lime, and peroxide of iron	15.44

The amount of fibrin has doubtless been overrated in both these analyses, since the coagulum contains lymph-corpuscles, and some albumen, in addition to that constituent. In Marchand's analysis it amounts to double the quantity in healthy blood. The quantity of albumen is also incorrectly stated, for a fluid containing  $\frac{43}{100}$  of albumen does not perfectly coagulate on heating, as this fluid is reported to have done, but merely becomes turbid, and deposits a few flocculi. The salts in Marchand's analysis amount to more than double the amount in the blood.

[L'Heretier (*Traité de Chimie Pathologique*, p. 18,) analysed the lymph obtained from the thoracic duct of a man who died from softening of the brain, and who took nothing but a little water for 30 hours preceding his death. It contained in 1000 parts:

Water	.	.	.	.	924.36
Solid constituents	.	.	.	.	75.64
Fibrin	.	.	.	.	3.20
Fat	.	.	.	.	5.10
Albumen	.	.	.	.	60.02
Salts	.	.	.	.	8.25]

Dr. Rees has published an analysis of the lymph taken from the absorbents of a young ass immediately after death. He states its constituents to be :

Water	.	.	.	.	.	.	965.36
Solid residue	.	.	.	.	.	.	34.64
Fibrin	.	.	.	.	.	.	1.20
Albumen	.	.	.	.	.	.	12.00
Extractive matter soluble in alcohol and in water	.	.	.	.	.	.	2.40
Extractive matter soluble in water only	.	.	.	.	.	.	13.19
Salts	.	.	.	.	.	.	5.85
Fat	.	.	.	.	.	.	a trace.

The salts were alkaline chlorides, sulphates, and carbonates, with traces of phosphates, and of peroxide of iron.

Lassaigne analysed lymph collected from the absorbents of the neck of a horse. He found in it, water 925.00, fibrin 3.30, albumen 57.36, chlorides of sodium and potassium, soda, and phosphate of lime 14.34.

[The lymph collected from the absorbent vessels of the neck of a horse has been recently analysed by Nasse. He obtained in 1000 parts :

Water	.	.	.	.	.	950.000	
Solid residue	.	.	.	.	.	50.000	
Albumen, with fibrin	.	.	.	.	.	39.111	
Water-extract	.	.	.	.	.	3.248	
Spirit-extract	.	.	.	.	.	0.877	
Alcohol-extract	.	.	.	.	.	0.755	
Ethereal extract	.	.	.	.	.	0.088	
Oleate of soda	.	.	.	.	.	0.575	} 5.611
Carbonate of soda	.	.	.	.	.	0.560	
Phosphate of soda	.	.	.	.	.	0.120	
Sulphate of potash	.	.	.	.	.	0.233	
Chloride of sodium	.	.	.	.	.	4.123	} 0.310
Carbonate of lime	.	.	.	.	.	0.104	
Phosphate of lime with some iron	.	.	.	.	.	0.095	
Carbonate of magnesia	.	.	.	.	.	0.044	
Silica	.	.	.	.	.	0.067	

It yielded no microscopic indications of urea. Nasse compared the lymph with the serum from the blood of a healthy horse, and found a remarkable coincidence in the salts of the two fluids :

	Serum.	Lymph.
Alkaline chlorides . . .	4·055	4·123
Alkaline carbonates <sup>1</sup> . . .	1·130	1·135
Alkaline sulphates . . .	0·311	0·233
Alkaline phosphates . . .	0·115	0·120
	<hr/> 5·611	<hr/> 5·611

The lymph, therefore, is a dilute serum, and the salts of the blood which make their escape along with the colourless *liquor sanguinis* from the capillaries, either return again in the same proportions to each other as they were secreted, into the capillaries, or, which is most probable, they only penetrate into the lymphatic vessels. Besides, there being more water in the lymph than in the serum (in the ratio of 950 to 922) the two fluids differ in the ratio of their solid constituents to the salts; in the lymph, the salts amount to 11·22, and in the serum to 9·65% of the solid residue. It is probably this circumstance that causes the much greater viscosity of the serum, which is by no means solely dependent on the larger quantity of albumen in solution.]

All investigations with respect to the motion of the lymph in the absorbents, and to the origin and formation of the lymph-corpuscles, have hitherto been comparatively fruitless. Since the primitive cells of the tissues are now regarded as organized individuals possessing self-dependent powers of selecting their own nutriment, and of discharging the function of secretion, we can no longer refer the passage of the lymph into the terminal points of the absorbents to mere physical endosmosis and exosmosis. I do not believe that we can altogether satisfactorily refer the motion of the lymph to a *vis a tergo*. Whether the lymph is propelled by a progressive contraction of the absorbent vessels, as is maintained by some physiologists, is uncertain; thus much, however, is undoubted, that there are numerous valves in the interior of the lymphatics to prevent the regurgitation of their fluid contents. From Weber's observations, it appears that in the tadpole the motion of the lymph is from 10 to 20 times slower than that of the blood.

<sup>1</sup> The oleate of soda is calculated as a carbonate.



*The Chyle.*

True chyle, that is to say, the emulsive fluid that is found after digestion in the lymphatic vessels of the intestinal canal, is usually turbid, and of a white or pinkish tint, but I once observed it of a blood-red colour. It is usually obtained for the purpose of analysis from the thoracic duct, when, although termed chyle, it is in reality a mixture of lymph and true chyle. Chyle, like lymph, coagulates in the course of from 8 to 15 minutes. The clot is soft, gelatinous, and either white (from the entangled fat-vesicles) or red (in consequence of the presence of blood-corpuscles.) The fibrin obtained by whipping fresh chyle is deficient in consistence, being sometimes merely gelatinous, and cannot be washed without suffering loss. The serum of the chyle appears, from my observations, (which were instituted with the chyle of horses) to contain four different sorts of corpuscles, viz. (*a*) fat-vesicles which occur in large numbers in milky chyle; (*b*) blood-corpuscles, which may be numerous, few, or absent, according to circumstances; (*c*) round, colourless, transparent, rarely granular globules, from one half to three fourths the size of blood-corpuscles; I have never observed them in the blood; they are the true lymph-corpuscles; and (*d*) round, gray or colourless granular corpuscles, with a clearly defined, and not tuberculated outline, half as large again, or occasionally even twice as large as the blood-corpuscles; these are the chyle-corpuscles, which are always found in the blood. Fig. 12 exhibits chyle containing numerous blood-corpuscles as seen under the microscope.

Human chyle has never yet been analysed, but several analyses of the chyle of the lower animals have been made. Through the kindness of Professor Gurlt I have had several opportunities of examining the chyle of horses, and I have made three careful quantitative analyses of it. The method of analysis was precisely the same as for the blood. The fibrin was removed in the usual manner, and washed. A known quantity of the serum was reduced to dryness, and the water thus determined; the residue was finely pulverized, and a portion repeatedly treated with ether, and afterwards with spirit of .915 in order to remove the fat. It was then boiled in water. The residual albumen was dried and weighed. The spirituous and aqueous

solutions were mixed and evaporated, and the residue treated with water and dilute spirit, which took up the salts and extractive matters, and left the hæmatoglobulin. The extractive matters were dried, weighed, and incinerated, and the salts thus determined.

The thoracic duct of a horse that had been kept without food for some time contained only a very small quantity of a reddish fluid, with an alkaline reaction, from which a slight fibrinous coagulum separated, and which, on standing, deposited a red sediment, while the supernatant fluid was clear and yellow. Blood-corpuscles were detected in the sediment, but they were not numerous, and, for the most part, altered in form. Lymph-corpuscles and a very few chyle-corpuscles were observed; some of the latter were of a remarkable size, and presented a resemblance to conglomerate fat-cells. 1000 parts of this chyle left a solid residue of 39·5, of which 20 consisted of albumen, and 3·2 of oily fat.

In order to obtain a larger supply of chyle, a horse was fed on peas steeped in water; it was shortly afterwards bled to death, and the chyle collected from the thoracic duct.

I obtained upwards of 600 grains of a reddish yellow alkaline fluid, which was immediately stirred, in order to separate the fibrin. In the serum there was comparatively little fat, and only a small number of blood-corpuscles; while, on the other hand, the lymph- and chyle-corpuscles were abundant. None of the large conglomerate cells observed in the former chyle could be detected.

The analysis of this chyle yielded:

	Analysis 55.
Water . . . . .	940·670
Solid constituents . . . . .	59·330
Fibrin . . . . .	0·440
Fat . . . . .	1·186
Albumen . . . . .	42·717
Hæmatoglobulin . . . . .	0·474
Extractive matters and salts . . . . .	8·360
Ptyalin, and globulin or casein, with chloride of sodium and lactate of soda . . . . .	1·780

The analysis of the salts was not carried out. The amount of solid constituents, and especially of albumen, is considerably larger than in the former instance, but the quantity of fat is remarkably small.

On a subsequent occasion I fed two horses with oats soaked in water, and analysed the chyle thus formed. Both specimens were stirred, in order to remove the fibrin: they had an alkaline reaction, but one was turbid and milky, containing an extraordinary amount of soft but firm fat, while the other was of a blood-red colour, and contained a considerable number of blood-corpuscles. Both specimens contained lymph- and chyle-corpuscles. I have endeavoured, in fig. 12, to represent the corpuscles that were observed in the blood-red chyle.

The analyses of these fluids yielded the following results :

	Analysis 56. Milky chyle.	Analysis 57. Blood-red chyle.
Water . . . . .	928·000	916·000
Solid constituents . . . . .	72·000	84·000
Fibrin . . . . .	0·805	0·900
Fat . . . . .	10·010	3·480
Albumen with lymph- and chyle-corpuscles	46·430	60·530
Hæmatoglobulin . . . . .	traces	5·691
Extractive matters . . . . .	5·320	5·265
Alkaline lactates and muriates, with traces of lime . . . . .	7·300	6·700
Sulphate and phosphate of lime and perox- ide of iron . . . . .	1·100	0·850

These analyses yield a much larger amount of solid constituents than those quoted above: the increase is especially observable in the amount of fat in the former, and in the conjoined amount of albumen and hæmatoglobulin in the latter of these analyses. There can be no doubt that these variations are due partly to the nature of the food, and partly to the manner in which chylopoiesis goes on in aged or diseased animals. The salts approximate closely, both in quality and quantity, with those that occur in the blood.

Dr. Rees analysed the chyle of the same ass to which reference has been already made in page 352. It contained :

Water . . . . .	902·37
Solid constituents . . . . .	97·63
Fibrin . . . . .	3·70
Fat . . . . .	36·01
Albumen . . . . .	35·16
Extractive matter soluble in alcohol and water	3·32
Extractive matter soluble in water only . . . . .	12·33
Salts (similar to those in the lymph) . . . . .	7·11

[Nasse<sup>1</sup> has instituted the following analysis of the chyle of the cat. It contained in 1000 parts :

Water . . . . .	905·7
Solid constituents . . . . .	94·3
Fibrin . . . . .	1·3
Fat . . . . .	32·7
Albumen, blood-corpuscles, and extractive matters . . . . .	48·9
Chloride of sodium . . . . .	7·1
Other soluble salts . . . . .	2·3
Iron . . . . .	traces
Earthy salts . . . . .	2·0 ]

The elaborate treatise of Tiedemann and Gmelin affords much information respecting the influence of diet on the qualities of the chyle, and on the modifications that it undergoes in its passage through the mesenteric glands.

Their analyses of the chyle of the horse are given in the following table :

	Water.	Solid constituents.	Clot.	Albumen.	Fat.	Spirit-extract, with salts.	Water-extract, with salts.
1	924·3	75·7	17·5	44·45	a trace	7·97	3·60
2	949·8	50·2	4·2	34·27	a little	8·41	2·33
3	918·3	81·7	7·8	42·86	16·12	11·83	2·04
4	967·9	32·1	1·9	19·32	a little	9·19	0·94
5	948·6	57·4	3·1	24·27	12·34	8·33	1·36
6	871·0	129·0	small	35·75	87·07		3·22
7	959·0	41·0		24·60 (?)	16·40 (?)		3·22

The first four analyses were made with chyle taken from the thoracic duct. The chyle in these cases separated into a bright red clot, and opaque, milky serum. The fifth analysis was made with chyle (taken from the same horse as in analysis 4) after its passage through the mesenteric glands, and the sixth analysis, with chyle, previous to its passage through them. In the former case, the chyle was of a bright red colour, and coagulated perfectly, forming a pale red clot, and a reddish white serum ; in the latter, it was white, and coagulated very imperfectly ; in fact, instead of there being a clot, there was merely a transparent yellowish film ; the serum was white and milky.

<sup>1</sup> Wagner's Handwörterbuch, vol. 1, p. 235, article 'Chylus.'



In the seventh analysis, the chyle was collected from the absorbents of the colon.

The fat in these various specimens of chyle was partly solid, and partly fluid; the salts were apparently the same as in the lymph. The albumen left about 2% of ash, which consisted of equal parts of carbonate and sulphate of lime, together with a little carbonate, hydrochlorate, and sulphate of soda. The dried clot in analysis 2, yielded 9.07% of brownish red ash, consisting of carbonate, sulphate, and muriate of soda, carbonate and phosphate of lime, and peroxide of iron.

Tiedemann and Gmelin have communicated the following data regarding the influence of diet on the chyle. Their experiments were made on dogs, and the chyle was taken from the thoracic duct.

1. After taking cheese the chyle coagulated very slightly. The clot was little more than a pale red transparent film, and the serum was slightly milky. The chyle contained water 950.3, clot 1.71, residue of serum 48.0.

2. After the use of starch, the chyle was of a pale yellowish white colour, and coagulated rapidly. It contained water 930.0, clot and residue of serum 70.0. The clot was of a pale red colour.

3. After taking flesh, and bread and milk, the chyle was of a reddish white colour, and coagulated rapidly, the clot being of a pale red tint and the serum very milky. It consisted of water 915.3, clot 2.7, and residue of serum 83.8.

4. After the use of milk, the chyle presented a milky appearance, and the clot was transparent and of a pale red colour.

5. After bread and milk, the chyle contained water 961.1, clot 1.9, and residue of serum 37.0.

6. After flesh, bread, and milk, the chyle was of a yellowish red colour, coagulated firmly, (separating into a bright red clot, and turbid yellow serum,) and contained water 933.5, clot 5.6, residue of serum 60.9.

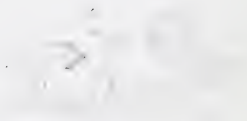
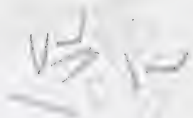
Any explanation of the results of these investigations would be superfluous, since it is obvious from them, that the food best adapted to dogs, viz. a mixture of flesh, bread, and milk,

yields the richest chyle, and increases the amount of clot. That the fibrin is formed in the chyle from the constituents of the food is perhaps less probable than that it is separated from the blood in the lymphatic glands; possibly, chyle of different qualities may react with varying energy on the lymphatic glands.

## EXPLANATION OF PLATE I.

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- Fig.* 1. Blood-corpuscles of men, birds, and amphibia.  
2. The formation of the blood-corpuscles, from Reichert.  
3. Urea precipitated from an alcoholic solution by nitric acid.  
4. Crystals produced in the alcohol-extract of blood devoid of urea, after the addition of nitric acid.  
5. Nitrate of urea from blood in morb. Brightii.  
6. Urea precipitated from an alcoholic solution, by oxalic acid.  
7. Crystals produced in the alcohol-extract of blood devoid of urea, after the addition of oxalic acid.  
8. Crystals of oxalic acid, resembling pure urea.  
9. Nitrate of soda.  
10. Crystalline groups of nitrate of urea, as it crystallizes from an alcoholic solution.  
11. Pus in blood.  
12. Chyle from the thoracic duct.







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 ELING, *near Southampton* . . . Spear, William, esq.  
 ELLAND, *Halifax* . . . Hamerton, John, esq.  
 Scholefield, John B. esq.
- ELTHAM, *Kent* . . . Guillemard, Isaac, M.D.  
 ELY . . . Muriel, John, esq.  
 EMSWORTH, *Hants* . . . Miller, George, esq.  
 ENFIELD, *Middlesex* . . . Miller, John, esq.  
 Taylor, William G. esq.
- EPPING . . . Merriman, Charles, A. esq.  
 EPSOM . . . Allan, John, esq.  
 Jones, Arthur O'Brien, esq.  
 Stillwell, George, esq.
- EVESHAM . . . Martin, Anthony, esq.  
 Porter, John H. M.D.
- EXETER, *Devon* . *Local Sec.* PENNELL, RICHARD LEWIN, M.D.  
 Blackall, John, M.D.  
 Delagarde, P. C. esq.  
 Empson, William, esq., Clist-Hydon  
 Granger, F. M.B.  
 Hall, William, M.D.  
 Kingdon, W. D. M.D.  
 Marsden, James, M.D.  
 Merry, W. H. esq., Broad Clyst  
 Miles, Erasmus, M.D., Heavitree  
 Parker, J. B. esq.  
 Shapter, Thomas, M.D.  
 Shaw, Henry, esq.
- EXMOUTH, *Devon* . . . Black, Glass, M.D.  
 Kane, William, esq.  
 Land, William H. esq.  
 Spettigue, John, esq.

FAIRFORD, <i>Gloucestershire</i>	. Cornwall, Charles, esq.
FALKIRK . . . . .	Espie, J. esq.
FALMOUTH . . . . .	Bullmore, F. C. esq.
FANET, <i>Ireland</i> . . . . .	Fullerton, J. W. esq.
FARRINGDON, <i>Berks.</i> . . . .	Mantell, George, M.D.
FARNINGHAM, near <i>Dartford</i>	Harris, Henry, esq.
	Hunt, F. B. M.D.
FARNHAM, <i>Surrey</i> . . . . .	Knowles, E. Y. esq.
	Newnham, William, esq.
FILEY, near <i>Scarboro', Yorks.</i>	Cortis, William S. esq.
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FOLKESTONE, <i>Kent</i> . . . . .	Minter,— esq.
FORFAR . . . . .	Steele, William, esq.
FOWEY, <i>Cornwall</i> . . . . .	Bennet, William P. esq.
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<i>cestershire</i> . . . . .	Watts, Thomas, esq.
FULBECK, <i>Grantham</i> . . . . .	Smith, Christopher B. esq.
GRAMPOUND, <i>Cornwall</i> . . . .	James, R. esq.
GARSTANG, <i>Lancashire</i> . . . .	Bell, William, M.D.
GATESHEAD . . . . .	Barkus, B. esq.
	Brady, H. esq.
	Dixon, G. esq.
GEDDING, <i>Woolpit, Suffolk</i> . .	White, W. Middleton, M.D.
GLASGOW . . . . . <i>Local Sec.</i>	FLEMING, J. G. M.D. 121, West Regent street
	Adams, J. M. esq.
	Anderson, Andrew, M.D.
	Anderson, A. D. M.D.
	Black, J. W. esq.
	Brown, James, M.D.
	Burns, John, M.D.
	Couper, John, M.D.
	Findley, John, M.D.
	Frazer, D. R.N.
	Gowdie, John, esq.
	Hall, Alfred, M.D.
	Hutcheson, William, M.D.
	Jeffray, James, M.D.
	Lancey, Thomas, esq.
	Laurie, J. A. M.D.
	Macewan, John, M.D.
	Macfarlane, John, M.D.
	Macneil, Neil, M.D.
	Mackie, Andrew, M.D.
	Maund, John, esq.
	Orr, R. S. M.D.
	Pagan, J. M. M.D.
	Parker, Robert, esq.
	Pollock, John, esq.
	Pritchard, Thomas, esq.
	Rainey, Harry, M.D.
	Smith, David, M.D.
	Thomson, William, M.D.
	<i>University Library, per Questor</i>
	Watson, James, M.D.
	Weir, William, M.D.
	Wright, William, esq.
GLASSLOUGH. <i>Co. of Monaghan</i>	Maffett, Richard, M.D.
GLoucester . . . . . <i>Local Sec.</i>	HITCH, S. M.D., Lunatic Asylum
	Cockin, John, esq.



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GODALMING . . .	Chandler, A. Thomas, esq.
GOOLE, <i>Yorkshire</i> . . .	Cass, William Eden, esq.
GOSPORT . . .	Jenkins, John, esq. Richardson, John, esq., Haslar Hospital Rundle, William John, M.D.
GRANTHAM . . .	Brown, Joseph, M.D.
GRAVESEND . . .	Armstrong, John, esq.
GREAT GRIMSBY, <i>Lincolnshire</i>	Keetley, Thomas Bell, esq.
GREAT YARMOUTH . . .	Worship, Harry, esq.
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HANLEY, <i>Staff.</i> . . .	Dale, James, esq.
HANWELL, <i>Middlesex</i> . . .	Begley, W. C. M.D., T. C. D.
HAREWOOD, <i>near Leeds</i> . . .	Smith, Gregory, esq.
HARLINGTON, <i>near Exeter</i> . . .	Cheesewright, William, esq.
HARROW-ON-HILL . . .	Curtis, H. Charles, esq. Hewlett, Thomas, esq.
HARROWGATE . . .	Berry, Grove, esq. Kennion, George, M.D. Stead, H. C. esq.
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HAWARDEN, <i>Flintshire</i> . . .	Moffat, John, M.D.
HELMSLEY, <i>York</i> . . .	Ness, John, esq.
HEMEL HEMPSTEAD, <i>Herts</i> . . .	Merry, Robert, esq.

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			Bull, Henry Graves, M.D.
			Cam, Thomas, esq.
			Farmer, John, esq.
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			Hanbury, George, esq.
			Lingen, Charles, esq.
			Lye, John Bleek, M.D.
			Scriven, John Barclay, esq.
			Smith, Robert, esq.
			Taylor, Theophilus, esq.
			Vevers, H. jun. esq.
			Waudby, Samuel, esq.
			Wright, Henry Goode, esq.
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			Phillips, George Marshall, esq.
			Reed, Frederick George, esq.
			Towers, G. A. esq., Infirmary
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HITCHIN	.	.	Foster, Oswald, esq.
			Shillitoe, R. R. esq.
HOLBEACH	.	.	Vise, E. B. esq.
HORBURY, <i>near Wakefield</i>	.	.	Robinson, Charles, esq.
HORNSEY	.	.	Hands, Benjamin, esq.
HORSFORTH, <i>near Leeds</i>	.	.	Wilson, William M. esq.
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			Martin, Thomas, esq.
			Coleman, W. T. M.D.
HOUGHTON-LE-SPRING, <i>Durham</i>			Green, Samuel, esq.
			Tweddell, William, esq.
HOUNSLOW	.	.	Emmott, C. B. esq.
HULL	.	Local Sec.	COOPER, HENRY, M.D.
			Clark, J. H. esq., Aldbrough
			Gordon, W. M.D.
			Hardey, Robert I. esq., Charlotte street
			Horner, F. R. M.D.
			Huntingdon, Frederick, esq.
			Locking, Jos. Agar, esq.
			Lunn, Wm. Jos. M.D.
			Riggall, Edward, esq.
			Sandwith, H. M.D.
			Sandwith, G. esq.
			Sharpe, Richard, esq., 9, Castle row
			Sharp, William, esq. F.R.S., Humber Bank
			Sleight, R. Leadam, esq.
			Twining, Edward, esq.
			Wallis, Edward, esq.
			West, Charles Turner, esq., 8, North street
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			Foster, M., <i>for Medical Library</i>
			Isaacson, Wootton, esq.
			Wilson, Josiah, esq.
HURSTPIERPOINT	.	.	Holman, Henry, esq.
HYDE	.	.	Tinker, William, esq.

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	Beck, Edward, M.D.
	Bullen, G. esq.
	Durrant, C. H. M.D.
	Scott, Walter, esq.
	Webster, W. H. B. esq.
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	Rowland, J. W. esq.
JARROW . . . .	Brown, W. W. esq.
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KENTON, <i>Devon</i> . . . .	Day, J. A. esq.
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	Jotham, George William, esq.
	Philbrick, Cornelius James, esq.
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	Taylor, Thomas, esq.
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	Paxton, John, M.D.
	Rodger, William, esq., Galston
	Thompson, John, esq.
	Young, Robert, esq.
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KINGTON, <i>Herefordshire</i> . . .	Marshall, G. Henry, esq.
KINGSTOWN, <i>Ireland</i> . . . .	Adams, William, M.D.
KIRKALDY, <i>Fifeshire</i> . . . .	Philp, John, esq.
KIRKHAM . . . .	Gradwell, William, esq.
	Shaw, Thomas, esq.
KIRKSTALL, <i>near Leeds</i> . . . .	Bishop, Edward, esq.
KNARESBOROUGH . . . .	Newton, Isaac, esq.
KNOWLE . . . .	Kimbell, J. H. esq.
KNUTSFORD, <i>Cheshire</i> . . . .	Gleeson, E. M. esq.
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	De Vitre, — M.D.
	Howitt, Thomas, esq.
	Ricketts, Charles, esq.
LEAMINGTON . . . .	Beesby, Ralph A. esq.
	Ebbage, Thomas, esq., Portland street
	Franklin, Francis, M.D.
	Jephson, J. M.D.
	Jones, Richard, esq.
	Starr, T. H. M.D.
LEATHERHEAD . . . .	Nash, William L. esq.
LEEDS . . . <i>Local Sec.</i>	TEALE, T. P. esq.
	Allanson, James, esq.
	Bearpark, G. E. esq.
	Braithwaite, W. esq.
	Brown, C. F. esq.
	Bulmer, George, esq.
	Cass, W. R. esq.
	Chadwick, Charles, M.D.
	Chorley, Henry, esq.

LEEDS ( <i>continued</i> )	Drennan, J. S. M.D. Evans, Evan, esq. Garlick, J. P. esq. Hall, Matthew, esq., Wortley Hay, William, jun. esq. Hey, Samuel, esq. Hey, William, esq. Hopper, R. S. M.D. Hobson, Richard, M.D. Irvine, G. W. M.D. Jackson, Matthew, esq. Land, Thomas, esq. <i>Leeds School of Medicine</i> Mayne, George, M.D. Morley, George, esq. Nunneley, Thomas, esq. Price, William, esq. Radcliffe, C. B. esq. Rickards, G. H. L. esq. Smith, Pyemont, M.D. Smith, Thomas, M.D. Staniland, Samuel, esq. Teale, Joseph, esq.
LEEK	Cooper, Richard, esq. Heaton, Charles, esq.
LENHAM	Stickings, George, esq.
LERWICK, <i>Shetland</i>	Cowie, John, esq.
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LIFF	Archibald, David, esq.
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LIVERPOOL ( <i>continued</i> ) .	<i>Liverpool Infirmary</i>
	Long, James, esq., 10 Rodney street
	Pearson, J. Armitage, esq. (Wootton)
	Smith, John Bromley, esq., 59, Great George street
	Swinden, Edward, esq., Wavertree
LLANDILO, <i>South Wales</i> .	Prothero, — M.D.
	Samuel, William, esq.

## LONDON LIST.

Abraham, Thomas, esq. .	49, Old Broad street, City
Adams, John, esq. .	31, New Broad street, City
Adcock, Christopher, esq. .	28, Charles terrace, New Cut, Lambeth
Addison, Thomas, M.D. .	24, New street, Spring gardens
Adlard, C. & J., Messrs. .	Bartholomew close
Allchin, W. H. esq. .	University College
Allen, W. esq. .	9, Albion place, Hyde park
Allhutt, Richard H. M.D. .	4, Parliament street
Ancell, Henry, esq. .	3, Norfolk crescent, Oxford square
Ansell, Thomas, esq. .	Bow
Appleton, H. esq. .	Lower Clapton
Archer, William, esq. .	1, Montague street, Portman square
Arnott, Neil, M.D. .	38, Bedford square
Ashley, W. H. esq. .	1, Grove villa, Loughboro' road, Brixton
Ashwell, Samuel, M.D. .	16, Grafton street, Bond street
Atkinson, John Charles, esq. .	Romney terrace, Westminster
Ayre, William, esq. .	Hackney
Babington, B. G. M.D. .	31, George street, Hanover square
Babington, R. esq. .	London University Hospital
Baker, Frederick M. esq. .	11, North place, Kingsland road
Balfour, Thomas Graham, M.D. .	St. James's square
Ball, R. de Champs, esq. .	12, Bloomsbury square
Ballard, Thomas, esq. .	81, Connaught terrace
Ballard, Edward, M.D. .	2, King Edward terrace, Islington
Bariff, F. esq. .	Portland place, Clapton
Barnes, Alfred, esq. .	Gloster house, King's road, Chelsea
Barnett, Thomas, esq. .	72, Fore street, Limehouse
Bartlett, William, esq. .	19, Notting hill terrace
Basham, William R. M.D. .	17, Chester street, Pimlico
Bateman, H. esq. .	9, Church row, Islington
Baxter, Henry F. esq. .	5, George street, Hanover square
Baylis, Edward, esq. .	30, Sackville street, Piccadilly
Beale, Miles, esq. .	Bishopsgate street
Bean, Edward, esq. .	Camberwell
Beane, Joseph M. esq. .	Peckham
Beck, J. S. esq. .	53, Upper Marylebone street, Portland place
Bell, Jacob, esq. .	338, Oxford street
Bennett, James Risdon, M.D. .	24, Finsbury place, north
Bentley, Edward, esq. .	35, Trinity square, Borough
Berry, Edward Unwin, esq. .	7, James street, Covent Garden
Bevan, Thomas, M.D. .	Finsbury circus
Bibby, Samuel, esq. .	9, North Audley street
Bird, James, esq. .	16, Orchard street, Portman square

Bird, Golding, M.D.	Myddleton square
Bird, Henry, esq.	Milan cottage, Hampstead road
Birkett, John, esq.	2, Broad street buildings
Birkett, E. L. M.B.	Cloak lane
Blenkarne, Henry, esq.	39, Dowgate hill
Blewitt, Octavian, esq.	73, Great Russell street, Bloomsbury
Blundell, James, M.D.	Great George street, Westminster
Bompas, Joseph C. esq.	University College
Bostock, John, M.D.	22, Upper Bedford place
Boyd, Robert, M.D.	Marylebone Infirmary
Bristowe, John Syer, esq.	Camberwell
Brodhurst, B. Edward, esq.	4, St. Helen's place, Bishopsgate.
Brodie, Sir Benjamin C. Bart.	14, Saville row
Brodribb, W. P. esq.	12, Bloomsbury square
Brown, C., Blakley, M.D.	3, John street, Berkeley square
Brown, Isaac Baker, esq.	39, Connaught terrace
Brown, J. Hallett, M.D.	7, St. George's place, Walworth road
Brown, R. F., esq.	2, St. Mary Axe
Brown, Robert, esq.	37, Euston square
Brown, Thomas, esq.	13, William street, Knightsbridge
Brown, Robert, esq.	Brixton hill
Brown, William, esq.	22, Russell place, Fitzroy square
Bryant, Walter, J. esq.	50, Edgeware road
Buchanan, G. A. esq.	50, Myddleton street, St. John street road
Buckland, J. Pelham, esq.	84, Watling street
Bull, Thomas, M.D.	27, Finsbury place
Burnett, Sir W. M.D. K.C.H.	The Admiralty
Burton, Henry, M.D.	41, Jernyn street
Bush, — M.D.	Kensington House
Butler, James, esq.	Seething lane, Tower street
Callaway, Thomas, esq.	Wellington street, London bridge
Campbell, Alex. Elliott, M.D.	First Life Guards
Camplin, John, esq.	11, Finsbury square
Camps, W. M.D.	50, Green street, Grosvenor square
Camps, W. M.D.	<i>for Parisian Medical Society</i>
Carr, James Thomas, esq.	St. Thomas's Hospital
Cartwright, Samuel, esq.	32, Old Burlington street
Chambers, William F., M.D.	46, Lower Brook street
Chepmall, E. C. M.D.	17, Hanover square
Chichester, J. H. R. esq.	3. Stone buildings, Lincoln's inn
Child, G. C. M.D.	Mortimer street
Cholmeley, W. esq.	St. Bartholomew's Hospital
Chowne, W. D., M.D.	Princes street, Cavendish square
Churchill, J. esq.	Princes street, Soho
Clark, Fred. Legros, esq.	Finsbury square
Clark, Sir James, Bart.	22 B, Lower Brook street
Clarke, J. F. esq.	23, Gerrard street, Soho
Cleland, A. esq.	118, Cock hill, Ratcliff
Clementson, F. L. esq.	6, Warwick Villas, Maida hill
Clendinning, John, M.D.	16, Wimpole street
Clifton, N. H. esq.	38, Cross street, Islington
Clissold, Rev. Augustus	Stoke Newington
Cochrane, J. G. esq.	London Library, 29, Pall Mall
Colebourne, Henry, esq.	28, Harleyford place, Kennington
Collyer, G. esq.	24, Old street road
Conquest, J. T. M.D.	13, Finsbury square
Cook, William, esq.	St. Thomas's hospital
Cooke, R. H. esq.	Church street, Stoke Newington
Cooke, William M. M.D.	Trinity square, Tower hill
Cooper, Bransby B. esq.	2, New street, Spring Gardens

Copland, James, M.D.	Old Burlington street
Cotton, R. Payne, esq.	11, Kensington square
Coulthred, James, esq.	4, Melton street, Southwark Bridge road
Courtenay, John, esq.	5, Finsbury terrace
Covey, Wm. Henry, esq.	42, Charing Cross
Coward, G. W. esq.	2, North Road, Hoxton
Cox, W. Travers, M.D.	2, Stanhope place
Craigie, J. L. esq.	Finsbury square
Crawford, Mervyn, M.D.	62, Upper Berkeley street
Crisp, Edwards, esq.	31, Beckford row, Walworth
Crompton, T. L. esq.	29, Howland street, Fitzroy square
Crowdy, Charles Whitton, esq.	Brixton hill
Crowther, J. R. esq.	6, Lansdown place, Brunswick square
Culpeper, William M. esq.	Marylebone Infirmary
Currie, Paul Francis, M.D.	30, Brook street
Curtis, J. W. esq.	Finsbury pavement
Dalrymple, John, esq.	56, Grosvenor street
Davies, Robert, esq.	126, Holborn Hill
Davies, David, esq.	St. Thomas's Hospital
Davis, J. Jones, M.B.	4, Poplar terrace, Poplar
Davis, Thomas, esq.	Hampstead
Davis, Richard Sladen, esq.	13, Chancery lane
Day, G. E. M.D.	3, Southwick street, Oxford square
De Morgan, Campbell, esq.	17, Manchester street
Dendy, Robert, esq.	2, Grafton street east, Tottenham Court road
Dendy, Walter C. esq.	10, Tillotson pl., Waterloo rd., <i>for Lond. Med. Soc.</i>
Derry, T. M. esq.	Westminster Hospital
Dewsnap, M. esq.	Hammersmith
Domeier, E. A. M.D., the late	39, University street
Dover, Frederick, esq.	54, Great Coram street
Duncan, Edward, esq.	3, Leadenhall street
Dunn, Robert, esq.	15, Norfolk street, strand
Duthoit, Thomas John, esq.	22, Trinidad place, Islington
Eddowes, J. H. esq.	St. Thomas's Hospital
Edwards, Henry, esq.	67, Edgeware road
Edwards, Vertue, esq.	St. Thomas's Hospital
Edwards, Daniel, esq.	13, Queen street, Cheapside
Ellam, John, esq.	320, Rotherhithe street
Erichsen, John, esq.	48, Welbeck street
Evans, J. O. esq.	University College
Eyles, John Brown, esq.	1, St. Andrew's court, Holborn
Eyles, Richard Strong, esq.	1, St. Andrew's court, Holborn
Eyre, Stratford A. esq.	3, Fitzroy street, Fitzroy square
Farr, William, esq.	Registrar-General's Office
Farre, Arthur, M.D.	Curzon street, May Fair
Farre, Frederick, M.D.	35, New Bridge street, Blackfriars road
Ferguson, Robert, M.D.	9, Queen street, May Fair
Fergusson, William, esq.	8, Dover street
Fidler, J. esq.	4, Camden row, Camberwell
Finch, Richard S. esq.	Marylebone Infirmary
Fincham, George, M.D.	38, Curzon street, May Fair
Fisher, J. W. esq.	Argyll street
Fitton, W. John, esq.	52, Upper Harley street
Fitzpatrick, Francis, esq.	27, Lisson street, New road
Foote, John, esq.	36, Tavistock street, Covent Garden
Forbes, John, M.D.	12, Old Burlington street
Fox, Charles James, M.D.	13, New Broad street, City
Frampton, Algernon, M.D.	29, New Broad street, City
France, John, esq.	88, Cadogan place
Fraser, Patrick S. M.D.	62, Guildford street

French, J. G. esq.	Marlborough street
Fuller, Hugh, esq.	53, King William street, City
Fuller, J. esq.	48, Hertford street, May Fair
Galton, Francis, esq.	16, King street, Covent Garden
Gardiner, John, esq.	49, Great Portland street
Gardiner, Roger Cooper, esq.	Cheyne walk, Chelsea
Garrett, Mark B. esq.	3, New Road, St. George's East
Garrod, A. B. M.D.	Charterhouse square
Gavin, Hector, M.D.	ThurLOW place, Hackney road
Gay, John, esq.	12, Finsbury Pavement
George, J. D. esq.	32, Old Burlington street
Gibson, John R. esq.	115, Holborn hill
Gillespie, Patrick, esq.	Lisson Grove north
Girdwood, Gilbert F. esq.	177, Maida hill
Godrich, Francis, esq.	Little Chelsea
Goodfellow, S. J. M.D.	London Fever Hospital
Goodwin, J. M. esq.	Streatham, Surrey
Goolden, R. H. M.D.	8, John street, Adelphi
Gordon, Adam, esq.	Surgeon R.N., 22, Surrey street, Strand
Grainger, R. D. esq.	St. Thomas's Hospital
Grant, N. M.D.	21, Thayer street, Manchester square
Grant, John, esq.	Bengal Army, 71 A, Grosvenor street
Gray, John, esq.	7, Upper George street, Portman square
Greenhalgh, Robert, esq.	66, Upper Charlotte street, Fitzroy sq.
Greenwood, Henry, esq.	Horsleydown lane
Griffith, J. W. M.D.	9, St. John's square
Grimsdale, Thomas F. esq.	University College
Guazzaroni, John, esq.	3, Terrace, Kensington
Guest, Edmund, esq.	College street, Chelsea
Gull, W. W. M.B.	Guy's Hospital
Gulliver, George, esq.	Roy. Reg. of Horse Guards
Gunthorpe, George John, esq.	51, Newington place, Kennington
Guy, W. A. M.B.	Bloomsbury square
Hakes, J. esq.	28, Duke street, Manchester square
Hall, Marshall, M.D.	14, Manchester square
Hamilton, Alfred, esq.	Broad street Buildings
Hanson, Sidney, M.D.	17, Hanover square
Harding, J. F. esq.	13, Spencer street, Northampton square
Hardwick, Alfred, M.D.	Kensington
Hardwicke, William, esq.	12, Calthorpe street, Gray's Inn road
Harper, Robert, esq.	2, Conduit street, Westbourne terrace, Hyde park
Harris, Wintow, esq.	1, New Dorset place, Clapham road
Harris, Michael, esq.	Paradise row, Hackney
Harston, A. D. esq.	Trinidad place, Islington
Hastings, John, M.D.	14, Albemarle street
Haviland, — M.D.	177, Maida hill
Hawkins, Cæsar, esq.	for Roy. Med. Chirurg. Soc. Berners street
Hawkins, James, esq.	36, Collett place, Commercial road
Hawkins, Charles, esq.	Albany Court yard
Headland, Edward, esq.	32, Guildford street
Heberden, W. M.D., the late	28, Cumberland street, Bryanstone square
Heming, G. O. M.D.	7 B, Manchester square
Henry, Alexander, esq.	4, Caroline street, Bedford square
Hensley, L. esq.	3, Great James street, Bedford square
Hering, William, esq.	14, Foley place
Herring, William, esq.	74, Sun street, Bishopsgate
Heisch, Frederick, jun., esq.	16, America square
Hilton, John, esq.	for Medical Library, Guy's Hospital
Hilton, John, esq.	Guy's Hospital
Hird, Francis, esq.	Cleveland row, St. James's



Hitchman, J. esq.	.	.	Sanatorium, New road
Hoar, W. esq.	.	.	78, Blackfriars road.
Hocken, Edward, M.D.	.	.	13, Bloomsbury square
Hodgkin, Thomas, M.D.	.	.	Brook street
Hodgson, Joseph, esq.	.	.	1, Spital square, Bishopsgate street Without
Holland, Henry, M.D.	.	.	23, Lower Brook street
Holman, William H. esq.	.	.	10, John street, America square
Holman, J. R. esq.	.	.	ditto
Holman, Charles H. esq.	.	.	ditto
Hopkins, John Morgan, M.D.	.	.	1, Elizabeth street, Eaton square
Houlton, Joseph, jun. esq.	.	.	87, Lisson grove North
Hovel, Thomas, esq.	.	.	Five Houses, Clapton
Howell, C. W. H. esq.	.	.	Stratford-le-Bow
Hughes H. M. M.D.	.	.	14, St. Thomas's street
Hulm, Edwyn St. James, M.D.	.	.	1, Tonbridge place, Burton crescent
Humby, Edwin, esq.	.	.	Warwick villa, Maida hill
Humphreys, William, esq.	.	.	21, Upper Southwick street
Hunt, Henry, M.D.	.	.	68, Brook street
Hutchinson, W. Barclay, esq.	.	.	40, Guildford street
Hutchinson, Francis, esq.	.	.	92, Farringdon street
Huxtable, William, esq.	.	.	1, Well's row, Hackney
Jackson, Alfred, esq.	.	.	London University College
Jackson, Thomas Carr, esq.	.	.	St. Thomas's Hospital
Jacob, William, esq.	.	.	31, Cadogan place
James, W. P. esq.	.	.	37, Euston square
James, Henry, esq.	.	.	4, City road
Jay, Henry, esq.	.	.	42, Sloane street
Jeaffreson, Henry, M.D.	.	.	2, Finsbury square
Jeaffreson, John F. esq.	.	.	Canonbury square, Islington
Jenkins, James, esq.	.	.	Royal Navy, 13, Clements lane
Jervis, Thomas, esq.	.	.	23, Edward street, Portman square
Jervis, George H. J. esq.	.	.	7, Kingsland green
Johnson, James, M.D.	.	.	8, Suffolk place, Haymarket
Johnson, Cavendish, esq.	.	.	3, Norfolk crescent
Jones, Thomas, M.D.	.	.	19, Finsbury pavement
Jones, Henry Derviche, esq.	.	.	23, Soho square
Jones, John Darlington, esq.	.	.	1, Queen's road, Dalston
Iliff, William T. esq.	.	.	18, Canterbury row, Newington Butts
Illingworth, Henry, esq.	.	.	1, Arlington street
Kaye, W. G. esq.	.	.	Royal Navy
Keen, Thomas, esq.	.	.	15, Manor place north, King's road, Chelsea
Kelsall, Thomas E. esq.	.	.	Great Winchester street, City
Kesteven, William, esq.	.	.	Upper Holloway
Keyser, A. esq.	.	.	21, Norfolk crescent, Burwood place
Kilner, John, esq.	.	.	33, Gower place, Euston square
King, Osman, esq.	.	.	37, Bernard street, Russell square
Kinnis, J. M.D.	.	.	Army
Lambert, H. esq.	.	.	St. Luke's Hospital, Old street road
Lammiman, R. W. esq.	.	.	118, Cock hill, Ratcliff
Lane, Samuel, esq.	.	.	1 Grosvenor place
Langmore, H. esq.	.	.	15, Upper George street, Portman square
Langmore, William, M.D.	.	.	Finsbury square
Langstaff, J. esq.	.	.	9, Cambridge square, Hyde Park
Lankester, Edwin, M.D.	.	.	19, Golden square
Latham, P. Mere, M.D.	.	.	36, Grosvenor street
Lauder, William P. M.D.	.	.	8, Sloane street
Law, Charles, esq.	.	.	3, Artillery place, Finsbury square
Leeson, H. B. M.D.	.	.	St. Thomas's Hospital
Lefevre, Sir George, M.D.	.	.	60, Lower Brook street, Grosvenor square
Leonard, Thomas, esq. M.B.	.	.	14, Aske terrace, Hoxton

Letheby, Henry, M.D.	London Hospital
Lever, J. C. W. M.D.	Wellington street, Borough
Lewis, David T. esq.	182, Brick lane, Spitalfields
Lewis, W. A. esq.	18, Stratford place, Cavendish square
Lister, Bryan, esq.	University College
Liston, Robert, esq.	Clifford street
Little, W. J. M.D.	Finsbury square
Lloyd, W. W. esq.	62, Great Russell street, Bloomsbury
Lobb, William, esq.	12, Aldersgate street
Lockley, Thomas, esq.	6, St. George's place, Hyde Park corner
Locock, Charles, M.D.	7, Hanover square
Luke, James, esq.	39, Broad street buildings
Lonsdale, Edward, esq.	for Library, Middlesex Hospital
Mackintosh, James, esq.	32, Wilton place, Knightsbridge
Macmeikan, John, esq.	London Hospital
MacLachlan, Daniel, M.D.	Chelsea Hospital
McGill, William, M.D.	2, Bentinck terrace, St. John's Wood
McGregor, Sir James, Bart.	13, St. James's place
McIntyre, William, M.D.	84, Harley street
Maillardet, J. W. esq.	8, St. Martin's place, Charing cross
Mann, John, esq.	63, Bartholomew close
Marshall, John, esq.	8, Crescent place, Mornington crescent
Marson, J. F. esq.	Resident Surgeon, Smallpox Hospital, Charing cross
Martin, J. R. esq.	71 A, Grosvenor street
Mathew, Charles Reeve, esq.	London University College
Mathew, James Edward, esq.	Church Cottage, De Beauvoir square, Kingsland
Mathews, R. N. B. jun. esq.	18, Canterbury row, Newington Butts
Mercer, Thomas E. esq.	University College, London
Meridith, E. F. esq.	15, Charles street, Westbourne terrace
Merriman, Jas. Nathaniel, esq.	Kensington
Merriman, John, esq.	Kensington
Merriman, S. W. J. M.D.	34, Brook street
Metcalfe, James B. esq.	Church street, Hackney
Miles, John, esq.	84, Harley street
Miles, John Shirley, esq.	8, Victoria square, Pimlico
Miller, C. M. esq.	1, Claremont terrace, Stoke Newington
Milroy, Gavin, M.D.	30, Fitzroy square
Moger, Robert, esq.	Highgate
Moore, Joseph, M.D.	10, Saville row
Morley, Atkinson, esq.	Burlington Hotel, Cork street
Munk, William, M.D.	2, Finsbury place, south
Murdock, William, M.D.	320, Rotherhithe street
Muriel, Charles, esq.	4, Wellington street, London bridge
Murphy, Edward W. M.D.	12, Henrietta street, Cavendish square
Nairne, Robert, M.D.	44, Charles street, Berkeley square
Nasmyth, Alexander, esq.	13 A, George street, Hanover square
Nelson, Duckworth, esq.	London Hospital
Newell, H. A. esq.	13, Warwick court, Holborn
Newton, Edward, esq.	26, Howland street
Nicolson, Thomas, esq.	53, Berkeley square
North, John, esq.	18, King street, Portman square
North, Robert Exton, esq.	26, Cheyne walk, Chelsea
Noys, G. H. M.D.	Moorgate street
Nussey, John, esq.	4, Cleveland row, St. James's
Olding, George, esq.	159, High street, Borough
Oldham, Henry, M.D.	13, Devonshire square, Bishopsgate
Ottley, Drewry, esq.	38, Hart street, Bloomsbury
Owen, Richard, esq.	College of Surgeons
Page, William E. M.D.	43, Curzon street, May Fair
Pardoe, George, M.D.	53, Russell square

Paris, John Ayrton, M.D.	. Dover street
Peacock, Thomas B. M.D.	. 2, South place, Finsbury
Percivall, W. esq.	. First Life Guards
Pereira, Jonathan, M.D.	. Finsbury square
Perigal, Frederick, esq.	. 33, Torrington square
Perkins, Dodd, esq.	. St. Thomas's Hospital
Perkins, Houghton, esq.	. Mortimer street, Cavendish square
Perry, James, esq.	. 4, Eaton square, Pimlico
Pettigrew, William V. M.D.	. 30, Chester street, Grosvenor place, Pimlico
Philp, Francis R. M.D.	. 28, Grosvenor street
Phillips, Benjamin, esq.	. 17, Wimpole street
Phillips, James, esq.	. White House, Bethnal green
Phillips, Thomas, esq.	. 44, Albion street, Hyde Park
Pilcher, George, esq.	. 7, Great George street, Westminster
Pitman, H. A. M.D.	. Montague place, Russell square
Poland, Alfred, esq.	. 21, Bow lane, Cheapside
Pout, George, esq.	. 65, High street, Borough
Powell, Henry, M.D.	. 31, Finsbury square
Powell, David, esq.	. 21, Garnault place, Spa Fields
Pyle, John, esq.	. 1, Middlesex place, New road
Quain, Richard, M.D.	. University College Hospital, Gower street
Quain, Richard, esq.	. 23, Kepple street
Redfearn, P. esq.	. 13½, Newington Causeway
Ree, Henry P. esq.	. Union place, City road
Reed, Septimus, esq.	. 41, Jewin street, City
Rees, Henry, esq.	. 45, Finsbury square
Reynolds, H. esq.	. 42, Moorgate street
Rhys, Thomas, esq.	. University College Hospital
Ridge, Joseph, M.D.	. 37, Cavendish square
Riding, Roger, M.D.	. 36, Euston square
Roberts, Charles I. M.D.	. 31, New Bridge street, Blackfriars
Roberts, John, esq.	. 34, Finsbury circus
Robins, William, esq.	. 16, Upper Southwick street
Robinson, James, esq.	. 7, Gower street
Robinson, Richard R. esq.	. 4, Camden row, Camberwell
Roods, Henry C. esq.	. 67, Great Russell street, Bloomsbury
Roots, H. S. M.D.	. Russell square
Rose, C. esq.	. 10, Barnes place, Mile end
Ross, Daniel, esq.	. 56, High street, Shadwell
Rowe, J. esq.	. 41, Upper John street, Fitzroy square
Rowley, R. M.D.	. 37, King William street, City
Royle, J. Forbes, M.D.	. 4, Bulstrode street, Cavendish square
Rust, Thomas, esq.	. 39, Connaught terrace
Rygate, John James, esq.	. London Hospital
Samwell, Francis, esq.	. Margaret street, Cavendish square
Sandon, James H. B. esq.	. 36, Albemarle street
Saunders, E. esq.	. 16, Argyle street
Savage, Henry, esq.	. 34, Dorset place, Dorset square
Savory, John, esq.	. 143, New Bond street
Sawer, Thomas, esq.	. 1, Lyon terrace, Maida hill
Scott, John, M.D.	. 12, Bedford square
Searle, G. C. esq.	. 42, Cumming street, Pentonville
Seaton, Edward, M.D.	. 77, Sloane street
Self, James, esq.	. Mile end road
Sharpe, Rd. esq.	. Grange road, Bermondsey
Sharpey, William, M.D.	. 35, Gloucester crescent, Regent's Park
Shute, Robert Greber, esq.	. 27, Mecklenburgh square
Skey, Fred. C. esq.	. 13, Grosvenor street
Smee, Alfred, esq.	. Finsbury circus
Smith, Henry, esq.	. 17, Henrietta street, Cavendish square

Smith, Ebenezer, esq.	Billiter square
Smith, John Simm, esq.	17, Trinity square, Tower hill
Solly, Samuel, esq.	1, St. Helen's place, Bishopsgate
Squibb, George James, esq.	6, Orchard street, Portman square
Squire, William, esq.	Wandsworth road
Statham, Hugh, esq.	Wandsworth road
Staunton, Charles F. M.D.	Royal Engineers, 40, St. Martin's lane
Stephen, T. esq.	King's College Library
Stewart, A. P. M.D.	130, Mount street, Berkeley square
Stewart, Haldane, esq.	55, Cadogan place
Stewart, Wm. Edward, jun. esq.	Weymouth street, Portland place
Stewart, Wm. esq.	1, Wells row, Hackney
Stocker, James, esq.	Guy's Hospital
Stokoe, Richard, esq.	Peckham Rye
Storks, Robert, esq.	44, Gower street
Stott, Thomas B. esq.	Aldersgate Dispensary
Stowers, Noel, esq.	26, Albion street, Hyde Park
Strickland, John, esq.	22, North Audley street
Sutherland, Alex. J. M.D.	19, Fludyer street, Westminster
Swaine, W. E. M.D.	41, Foley place
Synnett, — M.D.	8, Westbourne place, Eaton square
Tanner, Thomas Hawkes, esq.	King's College
Taunton, John C. esq.	48, Hatton garden
Taylor, Edward, esq.	Clapham Common
Taylor, W. esq.	London University Hospital
Taylor, C. esq.	18, Holland place, Clapham road
Taylor, Jas. Eastwood, esq.	4, Caroline street, Bedford square
Teavers, James, esq.	307, Rotherhithe wall
Teevan, William, esq.	23, Bryanstone square
Tegart, Edward, jun. esq.	37, Bryanstone street, Portman square
Thompson, Theophilus, M.D.	3, Bedford square
Thompson, Richard, esq.	<i>For London Institution, Finsbury</i>
Thomson, Anth. Todd, M.D.	30, Welbeck street
Thwaites, Thomas B. esq.	University College Hospital
Tibson, Arthur, esq.	1, Spring street, Paddington
Todd, Robert B. M.D.	26, Parliament street
Tomkins, C. Joseph, esq.	9, Huntley street, Bedford square
Toulmin, Frederick, esq.	Upper Clapton
Townsend, John A. esq.	48, Finsbury circus
Toynbee, John, esq.	Argyll place
Travers, Benjamin, esq.	Bruton street
<i>Treasurer of Medical Society</i>	University College, London
<i>Treasurer of St. George's Hospital Library</i>	
Tripe, John William, esq.	7, King's place, Bath street, Commercial road
Tulloh, James St. M.D.	3, Agar street, Strand
Turner, John, esq.	10, Bedford place, Russell square
Tweedie, Alexander, M.D.	30, Montague place, Bedford square
Ure, Alexander, esq.	13, Charlotte street, Bedford square
Vade, John Knox, M.D.	8, Upper Seymour street, Portman square
Varicas, R. A. esq.	29, Wobourne place, Tavistock square
Vaux, J. M.D.	Elm Cottage, Elm Grove, Hammersmith
Vincent, George, esq.	109, Sloane street
Vinen, Edward Hart, esq.	164, Blackfriars road
Waggett, John, M.D.	1, Norland terrace, Nottingham
Waite, Charles, esq.	3, Old Burlington street
Walcott, Robert Bowie, esq.	8, York street, Portman square
Walker, George A. esq.	101, Drury lane
Wall, John P. esq.	5, Mount street, Grosvenor square
Wallace, R. esq.	John's terrace, Hackney road
Walsh, Charles R. esq.	42, Half Moon street



Ward, Nathaniel, esq. .	7, Wellclose square, St. George's
Ward, N. Bagsshaw, esq. .	Ditto
Warder, A. W. esq. .	1, Upper York place, Fulham road
Ware, James T. esq. .	51, Russell square
Waterworth, Charles, esq. .	New Kent road, 5, Bengal place
Watson, Thomas, M.D. .	16, Henrietta street, Cavendish square
Weatherhead, Hume, M.D. .	63, Guildford street
Weber, Frederick, M.D. .	8, Grosvenor street
Webster, George, esq. .	78, Connaught terrace
Wells, Thomas Spencer, esq. R.N. .	36, Strand
Weston, Philip King, esq. .	11, Dalston terrace
Westwood, John, esq. .	Stepney
White, E. Stillingleet, esq. .	35, Edward square, Kensington
White, George, esq. .	50, Edgeware road
White, Frederick B. M.D. .	30, Nottingham place, Regent's Park
Whitney, W. U. esq. .	11, College street, Westminster
Whitwell, Francis, esq. .	Marylebone Infirmary
Wilks, G. A. F. M.D. .	19, Hart street, Bloomsbury
Williams, Allen, jun. esq. .	St. Thomas's street, Southwark
Williams, James, esq. .	Dalston terrace, Dalston
Williams, Charles J. B. M.D. .	7, Holles street, Cavendish square
Williamson, David, esq. .	26, Finsbury place
Willis, Robert, M.D. .	Dover street
Wilson, J. A. M.D. .	Dover street
Wilson, Erasmus, esq. .	Charlotte street, Fitzroy square
Wilson, Walter, esq. .	10, Everett street, Russell square
Winstanley, O. S. esq. .	7, Poultry
Woodfall, J. Ward, M.D. .	Dean's yard, Westminster
Wordsworth, J. C. esq. .	London Hospital
Wylie, John, esq. R.N. .	2, Aldermans walk, Bishopsgate
Yeldam, Stephen, esq. .	9, Stamford street, Blackfriars road
York, James, esq. .	Maida hill
Young, James Forbes, esq. .	Upper Kennington lane, Vauxhall
Young, Robert, M.D. .	Camberwell

LONDONDERRY . . .	Miller, Joseph Ewing, M.D.
LONG SUTTON, <i>Wisbeach</i> . .	Ewen, Henry, esq.
LOUGHBOROUGH, <i>Woodhouse, nr.</i>	Kennedy, James, M.D.
LOUTH, <i>Lincolnshire</i> . . .	Banks, John Tatam, M.D.
LOWESTOFFE . . . <i>Local Sec.</i>	WORTHINGTON, W. C., esq.
	Prentice, John, esq.
LUTTERWORTH . . . .	Buszard, Marston, esq.
	Walton, William, esq.
LYDD, <i>Kent</i> . . . .	Plomley, F. M.D.
LYNN REGIS, <i>Norfolk</i> . . .	De Mierre, Albert, M.D.
	Hunt, R. esq.
	Whiting, Joseph B. esq.
LYTHAM . . . .	Houghton, Edward, esq.
MACCLESFIELD . . . .	Holland, Loton, esq.
MAIDSTONE . . . <i>Local Sec.</i>	TAYLOR, GEORGE, M.D.
	Fry, Frederick, esq.
	Oates, T. V. esq.
	Ottley, John, esq.
	Prance, J. C. esq.
	Sanders, Godfrey, esq.
	Sibbald, William, M.D.
	Whatman, James, esq.

MALTON	.	.	<i>Local Sec.</i>	WRIGHT, JOHN JAMES, M.D. Bartliff, George, esq. Exley, John, M.D.
MANCHESTER	.	.	<i>Local Sec.</i>	NOBLE, DANIEL, esq., Piccadilly Aikenhead, John, M.D., Oxford street Ainsworth, R. F. M.D. Allen, Richard, esq. Bardsley, James L. M.D. Chatham street Barrow, Peter, esq., Clifford street Barton, Samuel, esq., Moseley street Beecvor, William Watson, esq., 43, Gt. George st. Birks, G. esq., Rosholme road Black, James, M.D., St. Peter's square Crompton, Samuel, esq., Grosvenor street Dorrington, Thomas, esq., Oxford road Goodlad, William, esq., the late, 46, Mosely street Greaves, George, esq. Hulme Hardy, Frederick, M.D. Henry, Mitchell, esq., Woodlands Holland, P. H. esq., Grosvenor street Howard, R. B. M.D. Hulme, J. D. M.D. Kerr, H. W. esq., Store street Mellor, Thomas, esq., Greenhays Noble, D. esq. <i>for Medical Society</i> Radford, Thomas, M.D., King street Richmond, Thomas Goodier, esq. Satterthwaite, Michael, M.D., Grosvenor street Turner, Thomas, esq., Mosely street Walker, John, esq., Princes street Watts, T. H. M.D., Dale street Welsh, W. H. M.D., Eccles Whitehead, James, esq., Oxford road Wilkinson, M. A. E. M.D., George street Williamson, W. C. esq. Upper Brook street Windsor, John, esq., Piccadilly
MARDEN, Kent	.	.	.	Perrey, Robert, esq.
MARKET BOSWORTH, Leicester	.	.	.	Evans, George, esq. Greary, Henry, esq. Lee, John, esq.
MARKET WEIGHTON, Yorkshire	.	.	.	Jackson, Matthew, esq.
MARLBOROUGH	.	.	<i>Local Sec.</i>	MAURICE, David P. esq.
MAYO	.	.	.	Clendinning, G. M.D.
MELFORD, LONG, Suffolk	.	.	.	Jones, Robert, esq.
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WESTON-SUPER-MARE	.	.	.	Burke, W. M. esq.
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WHITBY, <i>York</i>	.	.	.	Dowson, John, M.D.
WHITEHAVEN	.	.	.	Churchill, Jno. esq. <i>for Library.</i> King, R. F. esq. Wilson, Joseph, M.D.
WHITWELL, <i>near Welwyn, Herts.</i>				Butler, Thomas, esq.
WIMBORNE	.	.	.	Rowe, John, esq.
WINCHESTER	.	<i>Local Sec.</i>		WHITE, ARTHUR, M.D. Butler, Frederick, esq. Crawford, Andrew, M.D. Wickham, W. John, esq.
WINDSOR	.	<i>Local Sec.</i>		MAITLAND, CHARLES, M.D. Holderness, Wm. Brown, esq. Soley, T. A. esq., Thames street
WINTERTON, <i>near Brigg, Linc.</i>				Sadler, B. esq.
WIRKSWORTH	.	.	.	Poyser, Thomas, esq.
WISBEACH	.	.	.	England, W. M.D. Ewen, Henry, esq., Long Sutton
WISBOROUGH GREEN	.	.	.	Boxall, Henry, esq.
WOBURN, <i>Beds.</i>	.	.	.	Parker, T. esq.
WOLVERHAMPTON	.	<i>Local Sec.</i>		DEHANE, EDWARD FRANCIS, esq. Griffith, Samuel Hallett, esq.
WOODBIDGE, <i>East Soham</i>	.	.	.	Gross, Edward, esq.
WOOLWICH	.	<i>Local Sec.</i>		DENNE, WILLIAM, esq. Allinson, John Hiram, esq. Bisshipp, James, esq. Bossy, Francis, M.D. Butler, John, esq. Caryl, William Asylum, esq.

- WOOLWICH (*continued*) . . Dakin, William, esq.  
 Farr, George, esq.  
 Gant, Robert, esq.  
 Halifax, — M.D.  
 Stuart, William, esq.  
 Turner, James Samuel, esq.  
 Webb, Sir John
- WORCESTER . . . *Local Sec.* STREETEN, ROBT. J. N. M.D.  
 Addison, William, esq., Malvern  
 Day, Edmund, esq.  
 Hastings, Charles, M.D.  
 Hill, Richard, esq.  
 Jones, Walter, esq.  
 Malden, Jonas, M.D.  
 Nash, James, M.D.  
 Sheppard, James P. esq.  
 Turley, Edward A. esq.
- WRENBURY, *near Namptwich,*  
*Cheshire* . . . Thomson, David P. M.D.
- WREXHAM . . . Griffith, Thomas Taylor, esq.  
 Rowland, William, esq.  
 Williams, Edward, esq., Holt street
- WROTHAM, *Kent* . . . Kent, T. esq.
- WYCOMBE, *Bucks* . . . Rose, William, jun. esq.  
 Turner, John, esq.
- YALDING, *near Maidstone* . . . Pout, Henry, esq.
- YATTON, *near Bristol* . . . Lang, J. L. esq.
- YARMOUTH, *Isle of Wight* . . . Hollis, Charles Wise, M.D.
- YORK TOWN, *Bagshot, Surrey* . . Davies, William, esq.  
 Simpson, Frederick, esq.
- YORK . . . *Local Sec.* LAYCOCK, THOMAS, M.D.  
 Alderson, Septimus R. esq., Lunatic Asylum  
 Alderson, Richard R. esq.  
 Allen, Edmund T. esq.  
 Allen, Edward, esq.  
 Allen, James, esq.  
 Barker, Thomas H. esq.  
 Brunton, George, esq.  
 Dodsworth, Benjamin, esq.  
 Goldie, George, M.D.  
 Hodgson, Henry B. esq., Acomb House  
 Husband, William D. esq.  
 Keyworth, Henry, esq.  
*Library of York County Hospital*  
 Matternson, William, jun. esq.  
 Morris, Beverley R. M.D.  
 Proctor, William, esq. County Hospital  
 Reed, William, esq.  
 Russell, Henry, esq.  
 Scawin, William, esq.  
 Shann, George, M.D.  
 Simpson, Thomas, M.D.  
 Swineard, Frederick, esq.  
 Thomas, Richard, esq.  
 Thurnam, John, M.D., The Retreat  
 Walker, T. Kaye Lambe, esq.  
 Williams, Caleb, esq.
- YOUGHALL, *Co. Cork* . . . Desmond, John, M.D.

## FOREIGN LIST.

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Alexander, J. B. M.D.	. .	Indiana
Babington, W. F. esq.	. .	Bombay
Bee, — M.D.	. .	Tyro, Ohio
Beck, J. R. M.D.	<i>Local Sec.</i>	Albany
Bellingham, Wm. Henry, M.D.	.	Pisa
Boerstler, — M.D.	. .	Lancaster, Ohio
Bowen, W. S. esq.	. .	New York
Boyle, Alexander, M.D.	. .	St. John's, New Brunswick
Branham, R. H. M.D.	. .	Eatonton, Georgia
Brooks, J. W. M.D.	. .	Norwich
Burns, Robert, M.D.	. .	Frankford, Pennsylvania
Carpenter, — M.D.	. .	Lankaster, Pennsylvania
Carter, — M.D.	. .	Montreal
Chamberlaine, S. M.D.	. .	Baltimore, Maryland
Chermiside, Sir Robert, M.D.	. .	Paris
Cheyne, — M.D.	. .	Brizata, Columbia
Clapp, — esq.	. .	<i>for Pennsylvania Hospital</i>
Curwen, — M.D.	. .	Philadelphia
Dandridge, — M.D.	. .	Cincinnati, Ohio
Downie, Sir Alexander, M.D.	. .	Frankfort-on-Maine
Duncan, Edward, esq.	. .	Winchester, Kentucky
Dunglison, Robley, M.D.	<i>L. Sec.</i>	Philadelphia
Ermerins, — M.D.	. .	Groningen
Esby, William, esq.	. .	Washington
Fox, — M.D.	. .	Philadelphia
<i>Georgia Medical Society.</i>		
Giudice, Vittorio, M.D.	. .	Como
Green, H. M.D.	. .	New York
Hart, Samuel, esq.	. .	Charleston
Hay, Isaac, M.D.	. .	Philadelphia
Hecker, J. F. C. M.D.	. .	Berlin
Hodge, — M.D.	. .	Philadelphia
Huxton, — M.D.	. .	Philadelphia
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Johnstone, John M. esq.	. .	Georgetown, Demerara
Jones, — M.D.	. .	Philadelphia
King, Charles R. M.D.	. .	Philadelphia
Lajus, — M.D.	. .	Philadelphia
La Roache, — M.D.	. .	Philadelphia
Lea and Blanchard	. .	Philadelphia
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Macneven, W. H. M.D.	. .	New York
Macready, B. M. esq.	. .	New York
M'Pheeters, Wm. M. M.D.	. .	St. Louis, Missouri
Meigs, — M.D.	. .	Philadelphia
Mills, Maddison, M.D.	. .	New York
Mills, Charles S. esq.	. .	Richmond, Virginia
Mitchell, — M.D.	. .	Philadelphia
Moore, J. Wilson, M.D.	. .	<i>for College of Physicians, Philadelphia</i>



Morris, Casper, M.D.	Philadelphia
Mower, T. G. esq.	
Mütter, J. M.D.	Philadelphia
M'Vicar, John Augustus, M.D.	New York
Neville, — M.D.	Hamburgh
<i>New York Hospital</i>	
Norris, G. W. M.D.	Philadelphia
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Oppenheim, F. C. M.D.	Hamburgh
Overstreet, James, esq.	Washington
Pancoast, — M.D.	Philadelphia
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Patterson, H. S. M.D.	Philadelphia
Pepper, W. M.D.	Philadelphia
Perry, H. S. M.D.	Madeira
Roby, Joseph, M.D.	Maryland
Ross, Archibald Colquhoun, M.D.	Madeira
Rutherford, Henry Charles, M.D.	Caen, Normandy
Salter, Richard Henry, M.D.	Boston
Sands, A. B. M.D.	New York
Sargent, D. F. M.D.	Philadelphia
Sewall, Thomas, M.D. <i>Loc. Sec.</i>	Washington
Sievecking, Edward, M.D.	Hamburgh
Stewardson, — M.D.	Philadelphia
Stillé, Alfred, M.D.	Philadelphia
Stillé, Moreton, M.D.	Philadelphia
<i>Surgeon-General, United States.</i>	
Taylor, Isaac E. M.D.	New York
Taylor, Isaac E. M.D.	New York
Teulan, W. F. esq.	Halifax, N.S.
Tomes, Robert, M.D.	New York
Tripler, Charles . . esq.	
Wallace, Ellerslie, M.D.	Pennsylvania
Washington, James A. M.D.	New York
Wiley and Putnam, Messrs.	New York
Wood, G. B. M.D.	Philadelphia
Wood, Stephen, M.D.	New York

\* \* \* Although considerable pains have been taken to render this list as correct as possible, it is feared that some errors will be found. Of these the Secretary will be glad to receive information, in order that they may be corrected in future lists.





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Simon, Johann Franz  
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reference to the physiology  
and pathology of man

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